ON SOLUTIONS FOR THE MOVING BOUNDARY PROBLEM DESCRIBING AN ERODING VASCULAR GRAFT

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Synthetic accellular biodresorbable vascular grafts, which can degrade and vanish with time, are an important type of tissue engineered vascular grafts (TEVGs) with great clinical potential for blood vessel replacement surgeries. In order to study the *in vitro* degradation process of the graft in stationary solvent, a mathematical model is established using mixture theory. Balance laws and jump conditions across singular surfaces are used to determine the moving boundary conditions at surfaces of the vascular graft. The resulting system of equations is a moving boundary problem in the form of second order partial differential equations for the inner and outer domains. Regular perturbation theory is applied for both problems and first order solutions for the two moving boundaries are obtained. To test the accuracy of the approximate solutions, numerical solutions to the full problem are obtained and compared with the perturbation solutions. *In vivo*, degradation of the scaffold includes blood flow inside the inner domain. At the end of this thesis, we provide a formulation of this more general case.

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1.0 INTRODUCTION

Cardiovascular diseases are the main cause of mortality and a leading cause of impaired quality of life globally [1]. In spite of the development of advanced pharmacological and minimally-invasive techniques [2], surgeries with blood vessel replacement remain the choice for a large amount of patients [3], [4]. However, the autologous materials have a series of disadvantages including inconvenience of harvesting and preparing the graft, insufficient availability in patients with vascular diseases or in those who are receiving re-operations [5]. An alternative method that is receiving increasing attention is to use tissue engineering to manufacture the vessel replacement outside the human body, avoiding the need for material harvesting procedures for the patients.

Since Weinberg and Bell created the first well-recognized blood vessel substitute in 1986 [6], the evolution of tissue engineered vascular grafts (TEVGs) has provided a promising future for blood vessel replacement surgeries [7]–[9]. To date, there exists several types TEVGs including endothelial cell seeded synthetic grafts, collagen and fibrin-based vessels, cell self-assembly vessels, biodegradable synthetic vascular grafts, and decellularized scaffolds [10]. Among these approaches, biodegradable synthetic vascular grafts provide initial structure and strength for cellular attachment and infiltration and proliferation, and new blood vessels are reconstituted over time during the degradation process of the grafts. This array of TEVGs has advantages of customizable material property, low production cost, short production time, biocompatibility, and low risk of infection and rejection [5], [11]–[14]. However, even with these advantages, a high compatibility is required between the degradation of the grafts and the cellular growth and remodeling. If the degradation speed is too slow, it possibly leads to scar formation; if the degradation speed is too fast, the grafts may bulge out due to insufficient extracellular matrix (ECM). Moreover, Sugiura *et al.* [11] showed that there is a negative correlation between degradation speed and calcification, which may lead to thrombosis and graft rupture. Therefore the degradation process of biodegradable grafts need to be studied.

Mathematical models of the growth and remodeling process have been proposed to create prediction tools to model this process. In this thesis, we study the *in vitro* problem for a acellular biodegradable vascular graft eroded in stationary solvent. For the vascular degradation with cellular growth and remodeling, the framework of mixture theory is introduced to model this complex bio-process. In Chapter 2, we start from the derivation of balance of mass, balance of momentum, balance of energy as well as entropy inequality by following the works by Truesdell and Toupin [15], Bowen [16], and Ateshian [17]. Based on the balance laws and entropy inequality, we give the derivation for the jump conditions across singular surfaces. Many researchers have presented the derivation in their studies [18]–[21]. In this thesis, we derive the jump conditions by using the generalized Green-Gauss theorem and the generalized Reynolds' transport theorem given by Eringen [22].

In Chapter 3, we develop a mathematical model that describes the degradation process. We propose that the dissolution of the graft is driven by the concentration gradient, and this assumption is shown to be consistent with balance of mass for mixtures. According to Fick's law, we have

$$\mathbf{F} = -\mathbf{D}\nabla C \tag{1.1}$$

where $\mathbf{F}$ is the mass flux; C is the concentration; and $\mathbf{D}$ is the matrix of diffusivity. For convenience, it is assumed that all materials we consider are isotropic with respect to diffusion and that $\mathbf{D}$ is uniform and independent of C. Accordingly, Fick's second law is given by

$$\frac{\partial C}{\partial t} = D\nabla^2 C \tag{1.2}$$

where D is a scalar for isotropic diffusion.

The difficulty of this problem lies in the moving boundaries of the vascular graft because both the inner and outer radiuses of the graft are changing due to transfer of mass from the graft into the surrounding solution. This kind of problem with moving boundaries is also called Stefan problem, which was initially used to describe the melting of ice in water [23], [24]. For moving boundary problems, two boundary conditions are required at the moving boundaries [25]. In Chapter 3, a general governing equation is formulated for the problem by balance of mass, and jump conditions are used to obtain the moving boundary conditions and the Noyes-Whitney constitutive equation [26] is introduced as another boundary condition. Because of the existence of moving boundaries, the problem is analytically unsolvable in closed form. However, as an alternative, approximate

solutions are obtained by using perturbation theory. The key step for perturbation theory is to choose a small parameter ϵ by which the original problem can be expressed by infinite equation sets. If we make $\epsilon = 0$, the original problem may be reduced to a easy problem which is the zero$^{\text{th}}$ order problem. By solving this problem and substituting the zero$^{\text{th}}$ order solution into the original equation, higher order problems can be solved recursively. Vrentas [27] showed that if the parameters upon which the perturbation theory is based are small, the moving boundary moves slowly or not far from its initial position, and the error is also small for the approximate solutions. In Chapter 4, we obtain the zero$^{\text{th}}$ order solution of the concentrations and the first order solutions for the moving boundaries. A non-homogeneous linear partial differential equation set is given for higher order solutions from which high order solutions can be obtained recursively.

In Chapter 5, an implicit finite difference method is applied to obtain the numerical solutions to the full problem. Convergence is tested for the numerical approach to ensure the reliability. A comparison is made between the first order perturbation solutions and the numerical solutions. It is shown that the error of the first order solution for the moving boundaries are small. Therefore the validity of the approximate solutions is confirmed. The influence of two degradation parameters on the results is analyzed.

In Chapter 6, we consider the *in vivo* problem with blood flow inside the graft. The problem is necessarily extended to 2-dimensions since transport with blood flow involves axial dependence in addition to the radial dependence. By Fick's law and mixture theory, the flow problem is expressed by diffusion-convection equations based on a several assumptions. We also derived the moving boundary condition based on the study of Patel [28]. Although the solution for the problem is not obtained in this thesis, we present some valuable results from previous studies for this problem.

2.0 BALANCE LAWS AND JUMP CONDITIONS

Mixtures are materials which consist of two or more constituents. Truesdell and Toupin [15] introduced a theory for mixtures in 1960 including a derivation of balance laws. After that, Müller [18] employed Lagrange multipliers for mixtures of fluids, and Eringen and Ingram [19] presented the jump conditions for mixtures which consist of singular surfaces. For decades, mixture theory has been shown to be a powerful tool for studying complex mixtures. Even though mixtures can be described by simple continuum mechanics models, advantages of mixture theory arise if we need to study the properties and mechanisms for individual constituents. For biological tissues that may experience growth, breakdown, remodeling, and chemical reactions, mixture theory can simplify this complex bio-process into balance laws for each constituent [29], [30]. In this chapter, we give derivations for all balance laws, entropy inequality, and jump conditions in the forms following the presentation by Ateshian [17].

Now, consider a deformable continuous body $\mathcal{B}$ consisting of N constituents moving in a Euclidean space $\mathcal{R}$. The motion of each constituent is given by

$$\mathbf{x} = \boldsymbol{\chi}^{\alpha}(\mathbf{X}^{\alpha}, t) \tag{2.1}$$

where $\mathbf{X}^{\alpha}$ ($\mathbf{X}^{\alpha} \in \mathcal{B}$) is an arbitrary material point of constituent α at time t_0; $\mathbf{x}$ is the position vector that $\mathbf{X}^{\alpha}$ occupies at time t. If we use V_0 and V to denote the space occupied by $\mathcal{B}$ at time t_0 and t, respectively, the motion of the continuous body is shown in Figure 1.

The velocity of the material point $\mathbf{X}^{\alpha}$ is given by

$$\mathbf{v}^{\alpha} = \frac{\partial \boldsymbol{\chi}^{\alpha}}{\partial t} \tag{2.2}$$

Accordingly, the acceleration is

$$\mathbf{a}^{\alpha} = \frac{\partial^2 \boldsymbol{\chi}^{\alpha}}{\partial t^2} \tag{2.3}$$

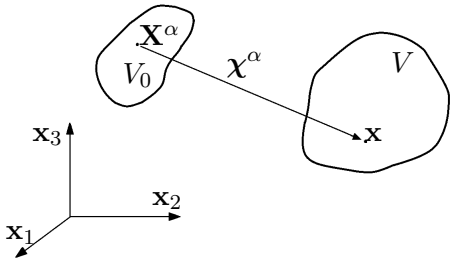


Figure 1: Motion of a continuous body $\mathcal{B}$.

If we consider an arbitrary scalar property f^{α} for constituent α, which is assumed to be described by

$$f^{\alpha} = f^{\alpha}(\mathbf{x}, t) \tag{2.4}$$

the material derivative of property f^{α} is defined by

$$\frac{Df^{\alpha}}{Dt} = \frac{\partial f^{\alpha}}{\partial t} + \nabla f^{\alpha} \cdot \mathbf{v} \tag{2.5}$$

where $\mathbf{v}$ is the mean velocity of the mixture to be defined later. Likewise, the material derivative of property f^{α} following the motion of constituent α is given by

$$\frac{D^{\alpha} f^{\alpha}}{Dt} = \frac{\partial f^{\alpha}}{\partial t} + \nabla f^{\alpha} \cdot \mathbf{v}^{\alpha} \tag{2.6}$$

In the following derivations in the balance laws and entropy inequality, we follow the derivation process given by Bowen [16]. However, instead of using a control volume as shown in his study, we use a material sub-region to make it consistent with the derivation of jump conditions presented by Eringen and Ingram [19].

2.1 BALANCE OF MASS

If chemical reactions are allowed, for an arbitrary material sub-region $\mathcal{V} \subseteq \mathcal{B}$, the mass variation for an individual constituent α in $\mathcal{V}$ is dominated by chemical reactions or phase transitions. In this case, the mass balance equation for the constituent α is given by [15]

$$\frac{d}{dt}\int_{\mathcal{V}^\alpha} \rho^\alpha \, dv = \int_{\mathcal{V}^\alpha} \hat{\rho}^\alpha \, dv \tag{2.7}$$

where ρ^α is the apparent density of constituent α at $\mathbf{x}$ and t; $\hat{\rho}^\alpha$ is the mass supply rate to constituent α from other constituents at $\mathbf{x}$ and t; $\mathcal{V}^\alpha$ is the material subregion coincident with $\mathcal{V}$ at time t proposed by Eringin and Ingram[1]. The total density of the subregion is defined by

$$\rho = \sum_\alpha \rho^\alpha \tag{2.8}$$

Therefore the mass of the subregion $\mathcal{V}$ is

$$\mathcal{M} = \int_{\mathcal{V}} \rho \, dv = \sum_\alpha \int_{\mathcal{V}^\alpha} \rho^\alpha \, dv \tag{2.9}$$

If we take the summation of Eqn.(2.7) over all constituents, and make use of Eqn.(2.8) and (2.9), we have

$$\frac{d\mathcal{M}}{dt} = \int_{\mathcal{V}^\alpha} \sum_\alpha \hat{\rho}^\alpha \, dv \tag{2.10}$$

which represents the mass change rate of the subregion $\mathcal{V}$. Moreover, according to the conservation of mass for a material region, (2.9) is equal to zero. As a result, the mass supply rate $\hat{\rho}^\alpha$ is subjected to

$$\sum_\alpha \hat{\rho}^\alpha = 0 \tag{2.11}$$

[1]Some authors, for example, Bowen, are not using $\mathcal{V}^\alpha$ in their research. We show the the definition of $\mathcal{V}^\alpha$ given by Eringen and Ingram [19] because it makes the presence of $\mathbf{v}^\alpha$ in Eqn.(2.12) more reasonable since we are using a material region approach. Some authors use other explanations for the $\mathbf{v}^\alpha$ term while not using the definition of $\mathcal{V}^\alpha$. Coussy [31] in his study used $\frac{d^\alpha}{dt}\int_{\mathcal{V}} f \, dv$ as the particle derivative following the motion of constituent α, and same result can be obtained.

The Reynolds' transport theorem corresponding to the subregion $\mathcal{V}^\alpha$ may be written as

$$\frac{d}{dt}\int_{\mathcal{V}^\alpha} f^\alpha \, dv = \int_{\mathcal{V}^\alpha} \left[\frac{\partial f^\alpha}{\partial t} + \nabla \cdot (f^\alpha \mathbf{v}^\alpha)\right] \, dv \tag{2.12}$$

By use of equations (2.6), (2.7), and (2.12), the local form of balance of mass is obtained as

$$\frac{D^\alpha \rho^\alpha}{Dt} + \rho^\alpha \nabla \cdot \mathbf{v}^\alpha = \hat{\rho}^\alpha \tag{2.13}$$

Moreover, if the relationship between a constituent property f^α and its corresponding mixture property f is described as

$$f = \frac{1}{\rho}\sum_\alpha \rho^\alpha f^\alpha \tag{2.14}$$

it can be shown that

$$\rho\frac{Df}{Dt} = \sum_\alpha \rho^\alpha \frac{D^\alpha f^\alpha}{Dt} - \nabla \cdot (\rho^\alpha f^\alpha \mathbf{u}^\alpha) + \hat{\rho}^\alpha f^\alpha \tag{2.15}$$

where $\mathbf{u}^\alpha$ is the diffusion velocity of constituent α defined by

$$\mathbf{u}^\alpha = \mathbf{v}^\alpha - \mathbf{v} \tag{2.16}$$

The balance of mass for individual constituents must be consistent with the balance of mass for the mixture. By taking the summation of Eqn.(2.13) over all constituents, we can show that it becomes

$$\frac{D\rho}{Dt} + \rho \nabla \cdot \mathbf{v} = 0 \tag{2.17}$$

which is the well recognized local form of balance of mass in continuum physics, where the mean velocity $\mathbf{v}$ of the mixture is defined by

$$\mathbf{v} = \frac{1}{\rho}\sum_\alpha \rho^\alpha \mathbf{v}^\alpha \tag{2.18}$$

2.2 BALANCE OF MOMENTUM

2.2.1 Balance of linear momentum

The balance of momentum for constituent α is given by [15]

$$\frac{d}{dt}\int_{\mathcal{V}^\alpha} \rho^\alpha \mathbf{v}^\alpha \, dv = \int_{\partial\mathcal{V}^\alpha} \mathbf{T}^\alpha \cdot \mathbf{n} \, da + \int_{\mathcal{V}^\alpha} \rho^\alpha \mathbf{b}^\alpha \, dv + \int_{\mathcal{V}^\alpha} (\hat{\mathbf{p}}^\alpha + \hat{\rho}^\alpha \mathbf{v}^\alpha) \, dv \tag{2.19}$$

where $\mathbf{T}^\alpha$ is the Cauchy stress tensor of α, and the first term in the right hand side containing $\mathbf{T}^\alpha$ represents the contact force from the mixture surrounding $\mathcal{V}^\alpha$; $\int_{\mathcal{V}^\alpha} \rho^\alpha \mathbf{b}^\alpha \, dv$ is the external body force exerted on constituent α; $\hat{\mathbf{p}}^\alpha$ is the momentum supply from other constituents inside $\mathcal{V}^\alpha$; $\hat{\rho}^\alpha \mathbf{v}^\alpha$ is the momentum supply due to mass supply from other constituents; and the term $\int_{\mathcal{V}^\alpha} (\hat{\mathbf{p}}^\alpha + \hat{\rho}^\alpha \mathbf{v}^\alpha) \, dv$ represents the complete local interaction inside $\mathcal{V}^\alpha$. Moreover, the supply term follows

$$\sum_\alpha (\hat{\mathbf{p}}^\alpha + \hat{\rho}^\alpha \mathbf{v}^\alpha) = 0 \tag{2.20}$$

For the left hand side of Eqn.(2.19), applying Reynolds transport theorem given in (2.12), we get

$$\frac{d}{dt}\int_{\mathcal{V}^\alpha} \rho^\alpha \mathbf{v}^\alpha dv = \int_{\mathcal{V}^\alpha} \left[\rho^\alpha \mathbf{a}^\alpha + \mathbf{v}^\alpha \left(\frac{D^\alpha \rho^\alpha}{Dt} + \rho^\alpha \nabla \cdot \mathbf{v}^\alpha \right) \right] \, dv \tag{2.21}$$

By substituting (2.21) and (2.13) into Eqn.(2.19), if we apply Gauss's divergence theorem to the contact force term and rearrange terms, the local form of the the balance of momentum is obtained as

$$\rho^\alpha \mathbf{a}^\alpha - \nabla \cdot \mathbf{T}^\alpha - \rho^\alpha \mathbf{b}^\alpha - \hat{\mathbf{p}}^\alpha = 0 \tag{2.22}$$

while the corresponding equation for the mixture is given by

$$\rho \mathbf{a} = \nabla \cdot \mathbf{T} + \rho \mathbf{b} \tag{2.23}$$

The mean acceleration $\mathbf{a}$ of the mixture is defined by

$$\mathbf{a} = \frac{D\mathbf{v}}{Dt} \tag{2.24}$$

and the mean body force density of the mixture is defined by

$$\mathbf{b} = \frac{1}{\rho} \sum_{\alpha} \rho^{\alpha} \mathbf{b}^{\alpha} \tag{2.25}$$

The Cauchy stress tensor $\mathbf{T}$ of the mixture is given by Bowen [16] as

$$\mathbf{T} = \mathbf{T}_{\mathrm{I}} + \sum_{\alpha} \rho^{\alpha} \mathbf{u}^{\alpha} \otimes \mathbf{u}^{\alpha} \tag{2.26}$$

$\mathbf{T}_{\mathrm{I}}$ is called the inner part of the stress tensor defined by

$$\mathbf{T}_{\mathrm{I}} = \sum_{\alpha} \mathbf{T}^{\alpha} \tag{2.27}$$

$\mathbf{T}$ is necessarily symmetric to satisfy the balance of angular momentum. Moreover, because $\rho^{\alpha}\mathbf{u}^{\alpha} \otimes \mathbf{u}^{\alpha}$ is symmetric, $\mathbf{T}_{\mathrm{I}}$ is also symmetric. It should be noted that $\mathbf{T}^{\alpha}$ may not be symmetric due to local interaction.

2.2.2 Balance of angular momentum

As proposed by Bowen [16], the balance of angular momentum for constituent α is given by

$$\frac{d}{dt} \int_{\mathcal{V}^{\alpha}} \mathbf{x} \times (\rho^{\alpha} \mathbf{v}^{\alpha}) \, dv = \int_{\partial \mathcal{V}^{\alpha}} \mathbf{x} \times (\mathbf{T}^{\alpha} \cdot \mathbf{n}) \, da + \int_{\mathcal{V}^{\alpha}} \left[\mathbf{x} \times (\rho^{\alpha} \mathbf{b}^{\alpha} + \hat{\mathbf{p}}^{\alpha} + \hat{\rho}^{\alpha} \mathbf{v}^{\alpha}) + \hat{\mathbf{m}}^{\alpha} \right] \, dv \tag{2.28}$$

where $\hat{\mathbf{m}}^{\alpha}$ is the moment of momentum supply vector that is first suggested by Truesdell and Toupin [15], then explored by Bowen [16]. The term $\int_{\partial \mathcal{V}^{\alpha}} \mathbf{x} \times (\mathbf{T}^{\alpha} \cdot \mathbf{n}) \, da$ represents the momentum from the contact force between $\mathcal{V}^{\alpha}$ and the mixture around it. The term $\int_{\mathcal{V}^{\alpha}} \left[\mathbf{x} \times (\hat{\mathbf{p}}^{\alpha} + \hat{\rho}^{\alpha} \mathbf{v}^{\alpha}) + \hat{\mathbf{m}}^{\alpha} \right] \, dv$ is the momentum caused by local interaction inside $\mathcal{V}^{\alpha}$. By applying Reynolds transport theorem

to the left hand side of Eqn.(2.28), we get

$$\frac{d}{dt}\int_{\mathcal{V}^\alpha} \mathbf{x}\times(\rho^\alpha \mathbf{v}^\alpha)\, dv = \int_{\mathcal{V}^\alpha} [\mathbf{x}\times\frac{\partial}{\partial t}(\rho^\alpha\mathbf{v}^\alpha) + (\mathbf{x}\times\mathbf{v}^\alpha)(\nabla\rho^\alpha\cdot\mathbf{v}^\alpha) + \mathbf{x}\times(\rho^\alpha\nabla\mathbf{v}^\alpha\cdot\mathbf{v}^\alpha) + (\rho^\alpha\nabla\cdot\mathbf{v}^\alpha)(\mathbf{x}\times\mathbf{v}^\alpha)]\, dv \tag{2.29}$$

By use of index notation, the first term inside integral in the right hand side of Eqn.(2.28) is written as

$$\int_{\partial\mathcal{V}^\alpha} \mathbf{x}\times(\mathbf{T}^\alpha\cdot\mathbf{n})\, da = \int_{\partial\mathcal{V}^\alpha} \varepsilon_{ijk}x_i T^\alpha_{jl} n_l \mathbf{e}_k\, da \tag{2.30}$$

where ε_{ijk} denotes the Levi-Civita symbol. For simplicity of discussion, a tensor $\mathbf{A}$ is defined through $A_{kl} = \varepsilon_{ijk}x_i T^\alpha_{jl}$, so that

$$\mathbf{A}\cdot\mathbf{n} = A_{kl}n_l\mathbf{e}_k = \varepsilon_{ijk}x_i T^\alpha_{jl} n_l \mathbf{e}_k \tag{2.31}$$

Therefore we can apply Green-Gauss theorem to Eqn.(2.30), and it becomes

$$\int_{\partial\mathcal{V}^\alpha} \mathbf{A}\cdot\mathbf{n} da = \int_{\mathcal{V}^\alpha} \nabla\cdot\mathbf{A}\, dv = \int_{\mathcal{V}^\alpha} (\varepsilon_{ijk}T^\alpha_{ji}\mathbf{e}_k + \varepsilon_{ijk}x_i\frac{\partial T^\alpha_{jl}}{\partial x_l}\mathbf{e}_k)\, dv \tag{2.32}$$

Next, we define a new vector $\mathbf{g}^\alpha = \varepsilon_{ijk}T^\alpha_{ji}\mathbf{e}_k$. By substituting $\mathbf{g}^\alpha$ into (2.32), we have

$$\int_{\partial\mathcal{V}^\alpha} \mathbf{A}\cdot\mathbf{n} da = \int_{\mathcal{V}^\alpha} (\mathbf{g}^\alpha + \mathbf{x}\times\nabla\cdot\mathbf{T}^\alpha)\, dv \tag{2.33}$$

and

$$\mathbf{g}^\alpha = \begin{pmatrix} T^\alpha_{32} - T^\alpha_{23} \\ T^\alpha_{13} - T^\alpha_{31} \\ T^\alpha_{21} - T^\alpha_{12} \end{pmatrix} \tag{2.34}$$

Hence, with the aid of (2.29) and (2.23), the balance law given in (2.28) may be written as

$$\int_{\mathcal{V}^\alpha} [\mathbf{x}\times\mathbf{v}^\alpha(\frac{D^\alpha\rho^\alpha}{Dt} + \rho^\alpha\nabla\cdot\mathbf{v}^\alpha - \hat{\rho}^\alpha) + \mathbf{x}\times(\rho^\alpha\mathbf{a}^\alpha - \nabla\cdot\mathbf{T}^\alpha - \rho^\alpha\mathbf{b}^\alpha - \hat{\mathbf{p}}^\alpha)]\, dv$$
$$= \int_{\mathcal{V}^\alpha} (\mathbf{g}^\alpha + \hat{\mathbf{m}}^\alpha)\, dv \tag{2.35}$$

It can be seen that the left hand side of Eqn.(2.35) can be eliminated using the balance of mass and the balance of linear momentum for individual constituents. Thus we obtain the local form of the balance of angular momentum, as

$$\hat{\mathbf{m}}^{\alpha} = -\mathbf{g}^{\alpha} \tag{2.36}$$

As a result,

$$\hat{\mathbf{m}}^{\alpha} = \begin{pmatrix} T^{\alpha}_{23} - T^{\alpha}_{32} \\ T^{\alpha}_{31} - T^{\alpha}_{13} \\ T^{\alpha}_{12} - T^{\alpha}_{21} \end{pmatrix} \tag{2.37}$$

For convenience, let us define

$$\hat{\mathbf{M}}^{\alpha} = (\mathbf{T}^{\alpha})^{\mathrm{T}} - \mathbf{T}^{\alpha} \tag{2.38}$$

and $\hat{\mathbf{M}}^{\alpha}$ is a skew-symmetric tensor, where

$$\hat{M}^{\alpha}_{32} = \hat{m}^{\alpha}_{1} \tag{2.39}$$

$$\hat{M}^{\alpha}_{13} = \hat{m}^{\alpha}_{2} \tag{2.40}$$

$$\hat{M}^{\alpha}_{21} = \hat{m}^{\alpha}_{3} \tag{2.41}$$

with the identity

$$\sum_{\alpha} \hat{\mathbf{M}}^{\alpha} = 0 \tag{2.42}$$

2.3 BALANCE OF ENERGY

The balance of energy for a constituent α is given by

$$\begin{aligned} \frac{d}{dt}\int_{\mathcal{V}^{\alpha}} \rho^{\alpha}(\varepsilon^{\alpha} + \frac{1}{2}\mathbf{v}^{\alpha}\cdot\mathbf{v}^{\alpha})\, dv = &\int_{\partial\mathcal{V}^{\alpha}} [\mathbf{v}^{\alpha}\cdot(\mathbf{T}^{\alpha}\cdot\mathbf{n}) - \mathbf{q}^{\alpha}\cdot\mathbf{n}]\, da \\ &+ \int_{\mathcal{V}^{\alpha}} [\mathbf{v}^{\alpha}\cdot(\rho^{\alpha}\mathbf{b}^{\alpha}) + \mathbf{v}^{\alpha}\cdot\hat{\mathbf{p}}^{\alpha} + \hat{\varepsilon} + \rho^{\alpha}\gamma^{\alpha} + \hat{\rho}^{\alpha}(\varepsilon^{\alpha} + \frac{1}{2}\mathbf{v}^{\alpha}\cdot\mathbf{v}^{\alpha})]\, dv \end{aligned} \tag{2.43}$$

where ε^α is the internal energy density for constituent α; $\mathbf{q}^\alpha$ is the heat flux vector; γ^α is the external heat supply; and $\hat{\varepsilon}^\alpha$ is the energy supply from other constituents. By use of the identity

$$\mathbf{v}^\alpha \cdot (\mathbf{T}^\alpha \cdot \mathbf{n}) = [(\mathbf{T}^\alpha)^{\mathrm{T}} \cdot \mathbf{v}^\alpha] \cdot \mathbf{n} \tag{2.44}$$

applying Reynolds transport theorem and Gauss's divergence theorem, Eqn.(2.43) becomes

$$\begin{aligned}\int_{\mathcal{V}^\alpha} [&(\varepsilon^\alpha + \frac{1}{2}\mathbf{v}^\alpha \cdot \mathbf{v}^\alpha)(\frac{\partial \rho^\alpha}{\partial t} + \rho^\alpha \nabla \cdot \mathbf{v}^\alpha + \mathbf{v}^\alpha \cdot \nabla \rho^\alpha - \hat{\rho}^\alpha) \\ &+ \mathbf{v}^\alpha \cdot (\rho^\alpha \frac{\partial \mathbf{v}^\alpha}{\partial t} + \rho^\alpha \nabla \mathbf{v}^\alpha \cdot \mathbf{v}^\alpha - \nabla \cdot \mathbf{T}^\alpha - \rho^\alpha \mathbf{b}^\alpha - \hat{\mathbf{p}}^\alpha) \\ &+ \rho^\alpha (\frac{\partial \varepsilon^\alpha}{\partial t} + \mathbf{v}^\alpha \cdot \nabla \varepsilon^\alpha) - \mathbf{T}^\alpha : \nabla \mathbf{v}^\alpha + \nabla \cdot \mathbf{q}^\alpha - \rho^\alpha \gamma^\alpha - \hat{\varepsilon}^\alpha] \, dv = 0\end{aligned} \tag{2.45}$$

By using the balance of mass and the balance of linear momentum for individual constituents, the first and the second terms in parenthesis in Eqn.(2.45) are identically zero. Thus we obtain the local form of balance of energy for constituent α as

$$\rho^\alpha \frac{D^\alpha \varepsilon^\alpha}{Dt} - \mathbf{T}^\alpha : \nabla \mathbf{v}^\alpha + \nabla \cdot \mathbf{q}^\alpha - \rho^\alpha \gamma^\alpha - \hat{\varepsilon}^\alpha = 0 \tag{2.46}$$

The balance of energy for the entire mixture is given by

$$\rho \frac{D\varepsilon}{Dt} = \mathbf{T} : \nabla \mathbf{v} - \nabla \cdot \mathbf{q} + \rho\gamma \tag{2.47}$$

where ε is the mean internal energy density of the mixture; $\mathbf{q}$ represents the heat flux vector; and γ represents the external heat supply. Like the stress tensor $\mathbf{T}$, ε and $\mathbf{q}$ are not simple superposition of the internal energy or heat fluxes of each constituent due to internal interaction. Following the study by Bowen [16], we define

$$\varepsilon = \varepsilon_{\mathrm{I}} + \frac{1}{\rho} \sum_\alpha \frac{1}{2} \rho^\alpha \mathbf{u}^\alpha \cdot \mathbf{u}^\alpha \tag{2.48}$$

$$\mathbf{q} = \mathbf{q}_{\mathrm{I}} + \frac{1}{2} \sum_\alpha \rho^\alpha (\mathbf{u}^\alpha \cdot \mathbf{u}^\alpha) \mathbf{u}^\alpha \tag{2.49}$$

and

$$\gamma = \frac{1}{\rho} \sum_\alpha \rho^\alpha \gamma^\alpha \tag{2.50}$$

Returning to the definitions of $\mathbf{q}$ and ε, it is noticed that both of the properties contain two parts. The first part is the internal part, and the second is the diffusion part related to diffusion velocity $\mathbf{u}^\alpha$. The inner part of of the internal energy density is given by

$$\varepsilon_{\mathrm{I}} = \frac{1}{\rho}\sum_\alpha \rho^\alpha \varepsilon^\alpha \tag{2.51}$$

while the inner part of the heat flux vector is defined by

$$\mathbf{q}_{\mathrm{I}} = \sum_\alpha [\mathbf{q}^\alpha - (\mathbf{T}^\alpha)^{\mathrm{T}} \cdot \mathbf{u}^\alpha + \rho^\alpha \varepsilon^\alpha \mathbf{u}^\alpha] \tag{2.52}$$

The above-mentioned definitions have to be consistent with the balance of energy. Namely, if we substitute (2.48)-(2.52) into the local form of the balance of energy of the mixture described by Eqn.(2.47), it can be expanded to the form for individual constituents given in Eqn.(2.46). Therefore that the diffusion velocity must yield

$$\sum_\alpha \rho^\alpha \mathbf{u}^\alpha = \mathbf{0} \tag{2.53}$$

Here, in particular, for the cases that the body force is uniform[2] , namely

$$\mathbf{b}^\alpha = \mathbf{b} \tag{2.54}$$

we may develop another way of describing the balance of energy. With the aid of (2.53), Eqn.(2.47) may be written as

$$\rho \frac{D\varepsilon}{Dt} = \mathbf{T} : \nabla \mathbf{v} - \nabla \cdot \mathbf{q} + \rho\gamma + \mathbf{b} \cdot \sum_\alpha \rho^\alpha \mathbf{u}^\alpha \tag{2.55}$$

It is noticed from (2.53) that the last term on the right of Eqn.(2.55) is zero. Next, if the body force is uniform, which is reasonable since the body force acting on most mixtures that we consider is gravity only, we may move $\mathbf{b}$ in the right hand side of Eqn.(2.55) inside the summation. Therefore Eqn.(2.55) can be further written as

$$\rho \frac{D\varepsilon}{Dt} = \mathbf{T} : \nabla \mathbf{v} - \nabla \cdot \mathbf{q} + \rho\gamma + \sum_\alpha \rho^\alpha \mathbf{u}^\alpha \cdot \mathbf{b}^\alpha \tag{2.56}$$

[2]All the following equations are derived with the assumption that the body force is uniform. However, Ateshian [17] showed same results without mentioning this assumption in his study.

The left side of Eqn.(2.56) can be expanded using (2.48),

$$\rho\frac{D\varepsilon}{Dt}=\rho\frac{D\varepsilon_{\mathrm{I}}}{Dt}+\sum_{\alpha}\left[\rho^{\alpha}\mathbf{u}^{\alpha}\cdot\frac{D^{\alpha}\mathbf{u}^{\alpha}}{Dt}-\nabla\cdot[(\frac{1}{2}\rho^{\alpha}\mathbf{u}^{\alpha}\cdot\mathbf{u}^{\alpha})\mathbf{u}^{\alpha}]+\frac{1}{2}\hat{\rho}^{\alpha}\mathbf{u}^{\alpha}\cdot\mathbf{u}^{\alpha}\right] \tag{2.57}$$

and the first term inside the parenthesis of (2.57) can be expressed as

$$\sum_{\alpha}\rho^{\alpha}\mathbf{u}^{\alpha}\cdot\frac{D^{\alpha}\mathbf{u}^{\alpha}}{Dt}=\sum_{\alpha}\rho^{\alpha}[\mathbf{u}^{\alpha}\cdot\mathbf{a}^{\alpha}-\nabla\mathbf{v}:(\mathbf{u}^{\alpha}\otimes\mathbf{u}^{\alpha})] \tag{2.58}$$

Then Eqn.(2.56) is expanded to

$$\begin{aligned}&\rho\frac{D\varepsilon_{\mathrm{I}}}{Dt}+\sum_{\alpha}\left[\rho^{\alpha}\mathbf{u}^{\alpha}\mathbf{a}^{\alpha}-\nabla\mathbf{v}:(\mathbf{u}^{\alpha}\otimes\mathbf{u}^{\alpha})-\nabla\cdot[(\frac{1}{2}\rho^{\alpha}\mathbf{u}^{\alpha}\cdot\mathbf{u}^{\alpha})\mathbf{u}^{\alpha}]+\frac{1}{2}\hat{\rho}^{\alpha}\mathbf{u}^{\alpha}\cdot\mathbf{u}^{\alpha}\right]\\&=(\mathbf{T}_{\mathrm{I}}-\sum_{\alpha}\rho^{\alpha}\mathbf{u}^{\alpha}\otimes\mathbf{u}^{\alpha}):\nabla\mathbf{v}-\nabla\cdot[\mathbf{q}_{\mathrm{I}}+\frac{1}{2}\rho^{\alpha}\mathbf{u}^{\alpha}\cdot\mathbf{u}^{\alpha})\mathbf{u}^{\alpha}]+\sum_{\alpha}\rho^{\alpha}\mathbf{u}^{\alpha}\cdot\mathbf{b}^{\alpha}+\rho\gamma\end{aligned} \tag{2.59}$$

For convenience, let us define a vector $\mathbf{k}$, where

$$\mathbf{k}=\sum_{\alpha}(\mathbf{q}^{\alpha}+\rho^{\alpha}\varepsilon^{\alpha}\mathbf{u}^{\alpha}) \tag{2.60}$$

and accordingly we have

$$\mathbf{T}_{\mathrm{I}}:\nabla\mathbf{v}=\sum_{\alpha}\mathbf{T}^{\alpha}:\nabla\mathbf{v}^{\alpha}+\sum_{\alpha}\mathbf{u}^{\alpha}\cdot\nabla\cdot\mathbf{T}^{\alpha}-\nabla\cdot\mathbf{k}+\nabla\cdot\mathbf{q}_{\mathbf{I}} \tag{2.61}$$

Now by substituting Eqn.(2.61) into (2.59), with the aid of the balance of linear momentum, we have

$$\rho\frac{D\varepsilon_{\mathrm{I}}}{Dt}=\sum_{\alpha}\mathbf{T}^{\alpha}:\nabla\mathbf{v}^{\alpha}-\nabla\cdot\mathbf{k}+\rho\gamma-\sum_{\alpha}\mathbf{u}^{\alpha}\cdot\hat{\mathbf{p}}^{\alpha}-\frac{1}{2}\sum_{\alpha}\hat{\rho}^{\alpha}\mathbf{u}^{\alpha}\cdot\mathbf{u}^{\alpha} \tag{2.62}$$

2.4 ENTROPY INEQUALITY

In this section, following the presentation by Bowen [16], we formulate the entropy inequality which represents the second axiom of thermodynamics. Unlike the balance of mass, momentum and energy of mixtures, the entropy inequality is not postulated for individual constituents since unrealistic constrains would be imposed on the mixture [17]. Based on the study by Bowen and

Wiese [32], the inequality of entropy is given by

$$\frac{d}{dt}\int_{\mathcal{V}^\alpha}\rho\eta\ dv \geqslant -\int_{\partial\mathcal{V}^\alpha}\sum_\alpha\frac{\mathbf{h}^\alpha}{\theta^\alpha}\cdot\mathbf{n}\ da+\int_{\mathcal{V}^\alpha}\sum_\alpha\frac{\rho^\alpha\gamma^\alpha}{\theta^\alpha}\ dv \tag{2.63}$$

where $\mathbf{h}^\alpha$ is an influx vector to be defined later, and θ^α is the temperature assigned to constituent α at $\mathbf{x}$, at t. If we apply Reynolds transport theorem with divergence theorem to (2.63) and get rid of the integral symbol, the local form of the inequality can be obtained as

$$\rho\frac{D\eta}{Dt}+\sum_\alpha\nabla\cdot\frac{\mathbf{h}^\alpha}{\theta^\alpha}-\sum_\alpha\frac{\rho^\alpha\gamma^\alpha}{\theta^\alpha}\geqslant 0 \tag{2.64}$$

where η is the entropy density of the mixture defined by

$$\eta=\frac{1}{\rho}\sum_\alpha\rho^\alpha\eta^\alpha \tag{2.65}$$

and η^α is the entropy density for constituent α.

Using (2.65), Eqn.(2.64) may be expanded to

$$\sum_\alpha[\rho^\alpha\frac{D^\alpha\eta^\alpha}{Dt}+\nabla\cdot(\frac{\mathbf{h}^\alpha}{\theta^\alpha}-\rho^\alpha\eta^\alpha\mathbf{u}^\alpha)-\frac{\rho^\alpha\gamma^\alpha}{\theta^\alpha}+\hat{\rho}^\alpha\eta^\alpha]\geqslant 0 \tag{2.66}$$

Next, with the aid of the local form of the balance of energy given in Eqn.(2.46), the term $\rho^\alpha\gamma^\alpha$ is replaced in (2.66). Therefore Eqn.(2.66) becomes

$$\begin{aligned}\sum_\alpha\Big[&\rho^\alpha\frac{D^\alpha\eta^\alpha}{Dt}+\frac{1}{\theta^\alpha}\nabla\cdot\mathbf{h}^\alpha-\frac{\mathbf{h}^\alpha\cdot\nabla\theta^\alpha}{(\theta^\alpha)^2}-\nabla\cdot(\rho^\alpha\eta^\alpha\mathbf{u}^\alpha)\\&-\frac{1}{\theta^\alpha}[\rho^\alpha\frac{D^\alpha\varepsilon^\alpha}{Dt}-\mathbf{T}^\alpha:\nabla\mathbf{v}^\alpha+\nabla\cdot\mathbf{q}^\alpha-\hat{\varepsilon}^\alpha]+\hat{\rho}^\alpha\eta^\alpha\Big]\geqslant 0\end{aligned} \tag{2.67}$$

By introducing a new scalar $\hat{e}^\alpha$ which is defined by

$$\hat{e}^\alpha=\hat{\varepsilon}^\alpha+\mathbf{u}^\alpha\cdot\hat{\mathbf{p}}^\alpha+\hat{\rho}^\alpha(\varepsilon^\alpha+\frac{1}{2}\mathbf{u}^\alpha\cdot\mathbf{u}^\alpha) \tag{2.68}$$

Eqn.(2.67) is written as

$$\begin{aligned}\sum_\alpha\frac{1}{\theta^\alpha}[&\rho^\alpha(\theta^\alpha\frac{D^\alpha\eta^\alpha}{Dt}-\frac{D^\alpha\varepsilon^\alpha}{Dt})+\mathbf{T}^\alpha:\nabla\mathbf{v}^\alpha-\frac{\mathbf{h}^\alpha\cdot\nabla\theta^\alpha}{\theta^\alpha}+\nabla\cdot(\mathbf{h}^\alpha-\mathbf{q}^\alpha)-\theta^\alpha\nabla\cdot(\rho^\alpha\eta^\alpha\mathbf{u}^\alpha)\\&-\hat{\rho}^\alpha(\varepsilon^\alpha-\theta^\alpha\eta^\alpha+\frac{1}{2}\mathbf{u}^\alpha\cdot\mathbf{u}^\alpha)+\hat{e}^\alpha-\mathbf{u}^\alpha\cdot\hat{\mathbf{p}}^\alpha]\geqslant 0\end{aligned} \tag{2.69}$$

At this point, the definition of the flux vector $\mathbf{h}^\alpha$ given by Bowen [16] is

$$\mathbf{h}^\alpha = \mathbf{q}^\alpha + \theta^\alpha \rho^\alpha \eta^\alpha \mathbf{u}^\alpha \tag{2.70}$$

By substituting (2.70) into (2.63), the general form of the entropy inequality for individual constituents is obtained, which is rewritten as

$$\int_{\mathcal{V}^\alpha} \frac{\partial}{\partial t}(\rho\eta)\, dv \geqslant -\int_{\partial\mathcal{V}^\alpha} \sum_\alpha \rho^\alpha \eta^\alpha \mathbf{v}^\alpha \cdot \mathbf{n}\, da - \int_{\partial\mathcal{V}^\alpha} \sum_\alpha \frac{\mathbf{q}^\alpha}{\theta^\alpha} \cdot \mathbf{n}\, da + \int_{\mathcal{V}^\alpha} \sum_\alpha \frac{\rho^\alpha \gamma^\alpha}{\theta^\alpha}\, dv \tag{2.71}$$

Moreover, inequality (2.69) may be written as

$$\begin{aligned}\sum_\alpha \frac{1}{\theta^\alpha}[\rho^\alpha(\theta^\alpha \frac{D^\alpha \eta^\alpha}{Dt} - \frac{D^\alpha \eta^\alpha}{Dt}) + \mathbf{T}^\alpha : \nabla \mathbf{v}^\alpha - \\ \frac{1}{\theta^\alpha}(\mathbf{q}^\alpha \cdot \nabla\theta^\alpha) + \hat{e}^\alpha - \mathbf{u}^\alpha \cdot \hat{\mathbf{p}}^\alpha - \hat{\rho}^\alpha(\varepsilon^\alpha - \theta^\alpha\eta^\alpha + \frac{1}{2}\mathbf{u}^\alpha \cdot \mathbf{u}^\alpha)] \geqslant 0\end{aligned} \tag{2.72}$$

For mixtures subjected to a uniform temperature, we may obtain an alternative form of the inequality. To this end, we introduce the Helmholtz free energy which is defined by

$$\psi^\alpha = \varepsilon^\alpha - \eta^\alpha \theta^\alpha \tag{2.73}$$

and the material derivative of ψ following the motion of constituent α is

$$\frac{D^\alpha \psi^\alpha}{Dt} = \frac{D^\alpha \varepsilon^\alpha}{Dt} - \eta^\alpha \frac{D^\alpha \theta^\alpha}{Dt} - \theta^\alpha \frac{D^\alpha \eta^\alpha}{Dt} \tag{2.74}$$

By substituting (2.74) back into Eqn.(2.72), with the understanding that $\theta^\alpha = \theta$, we obtain

$$\begin{aligned}\sum_\alpha [-\rho^\alpha(\frac{D^\alpha \psi^\alpha}{Dt} + \eta^\alpha \frac{D^\alpha \theta}{Dt}) \\ + \mathbf{T}^\alpha : \nabla \mathbf{v}^\alpha - \frac{1}{\theta}(\mathbf{q}^\alpha \cdot \nabla\theta) + \hat{e}^\alpha - \mathbf{u}^\alpha \cdot \hat{\mathbf{p}}^\alpha - \hat{\rho}^\alpha(\psi^\alpha + \frac{1}{2}\mathbf{u}^\alpha \cdot \mathbf{u}^\alpha)] \geqslant 0\end{aligned} \tag{2.75}$$

Moreover, if the mixture is subjected to a uniform body force, it can be shown that

$$\sum_\alpha \hat{e}^\alpha = 0 \tag{2.76}$$

Therefore the entropy inequality is further reduced to

$$\sum_{\alpha}[-\rho^{\alpha}(\frac{D^{\alpha}\psi^{\alpha}}{Dt}+\eta^{\alpha}\frac{D^{\alpha}\theta}{Dt})+\mathbf{T}^{\alpha}:\nabla\mathbf{v}^{\alpha}-\frac{1}{\theta}(\mathbf{q}^{\alpha}\cdot\nabla\theta)-\mathbf{u}^{\alpha}\cdot\hat{\mathbf{p}}^{\alpha}-\hat{\rho}^{\alpha}(\psi^{\alpha}+\frac{1}{2}\mathbf{u}^{\alpha}\cdot\mathbf{u}^{\alpha})]\geqslant 0 \quad (2.77)$$

2.5 JUMP CONDITIONS

In the derivations of the balance of mass, momentum and energy, and the entropy inequality, we utilize the Reynolds' transport theorem and Green-Gauss divergence theorem to obtain the local form. However, this requires that the properties of the mixture are continuous inside $\mathcal{V}$. If, in particular, some properties inside $\mathcal{V}$ suffer a discontinuity, we need more general expressions for both the Reynolds' transport theorem and the Green-Gauss theorem. Conventionally, we call the surfaces, across which discontinuities happen, singular surfaces. In our problem, the surfaces of the graft are considered to be singular surfaces since it suffers jumps in both density and material velocity. Here, as defined by Casey [33], a singular surface is a mathematical representation of infinitesimally narrow region across which changes occur in some field properties of the medium. Those properties can be temperature, velocity, density, pressure, etc, though not motion. In other words, a gap or overlap is not allowed inside $\mathcal{V}$. Figure 2 shows the concept of a singular surface. The singular surface Γ is defined to be a function of time. Normally, it is irrelevant to the motion of $\mathcal{V}$ and not always material [33]. The approach for deriving jump conditions is to analyze properties in $\mathcal{V}_1$ and $\mathcal{V}_2$ separately with the understanding that $\mathcal{V}$ is still a material region subjected to all the balance laws and the entropy inequality [20], [21].

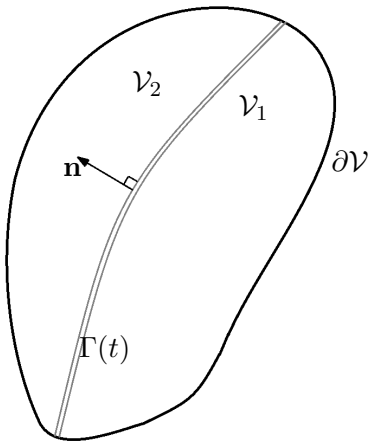


Figure 2: A singular surface $\Gamma(t)$ divides a material region $\mathcal{V}$ into two subregions $\mathcal{V}_1$ and $\mathcal{V}_2$. $\partial\mathcal{V}$ is the surface of $\mathcal{V}$; $\mathbf{n}$ is the unit normal on $\Gamma(t)$ which points into $\mathcal{V}_2$ side.

If numbers 1 and 2 are used to describe properties in $\mathcal{V}_1$ and $\mathcal{V}$, the jump for an arbitrary field property Φ is defined by

$$[[\Phi]] = \Phi_2 - \Phi_1 \tag{2.78}$$

For a region $\mathcal{V}^\alpha$ with singular surface $\Gamma(t)$, the generalized Green-Gauss theorem and Reynolds' transport theorem are given by Eringen [22] as

$$\int_{\partial\mathcal{V}^\alpha} \mathbf{f}^\alpha \cdot \mathbf{n}\, da = \int_{\mathcal{V}_1^\alpha + \mathcal{V}_2^\alpha} \nabla \cdot \mathbf{f}^\alpha\, dv + \int_{\Gamma(t)} [[\mathbf{f}^\alpha]] \cdot \mathbf{n}\, da \tag{2.79}$$

$$\frac{d}{dt}\int_{\mathcal{V}^\alpha} \rho^\alpha f^\alpha\, dv = \int_{\mathcal{V}_1^\alpha + \mathcal{V}_2^\alpha} \left[\frac{\partial}{\partial t}(\rho^\alpha f^\alpha) + \nabla \cdot (\rho^\alpha f^\alpha \mathbf{v}^\alpha)\right] dv + \int_{\Gamma(t)} [[\rho^\alpha f^\alpha \mathbf{u}_\Gamma^\alpha]] \cdot \mathbf{n}\, da \tag{2.80}$$

where f^α is an arbitrary scalar property and $\mathbf{f}^\alpha$ is an arbitrary tensor property, and

$$\mathbf{u}_\Gamma^\alpha = \mathbf{v}^\alpha - \mathbf{v}_\Gamma \tag{2.81}$$

where $\mathbf{v}_\Gamma$ is the velocity of the singular surface.

The following derivations follow the work by Eringen and Ingram [19] with some variations in notations.

2.5.1 Jump of mass

Because the material region is divided by a singular surface, from now on, we analyze the jump conditions by regarding $\mathcal{V}$ as two connected regions as shown in Figure 2. It is noticed that $\mathcal{V}_1$ and $\mathcal{V}_2$ are not material regions and there are mass, momentum, and energy supplies generated on the singular surface. Thus we can expand the mass supply rate for constituent α inside $\mathcal{V}$ as

$$\int_{\mathcal{V}^\alpha} \hat{\rho}^\alpha \, dv = \int_{\mathcal{V}_1^\alpha + \mathcal{V}_2^\alpha} \hat{\rho}^\alpha \, dv + \int_{\Gamma(t)} \bar{\rho}^\alpha \, da \tag{2.82}$$

Here, the physical meaning of $\bar{\rho}^\alpha$ is the mass supply rate per area to constituent α from other constituents on the singular surface $\Gamma(t)$. By taking the summation of (2.82) over all constituents and using the balance of mass, we have

$$\sum_\alpha \bar{\rho}^\alpha = 0 \tag{2.83}$$

One example is ice melting in liquid water, where the singular surface is the interface between ice and water. There are two constituents which are ice and water. For the ice phase, particularly, $\bar{\rho}^\alpha$ represents the mass removal of ice due to melting, while $\bar{\rho}^\alpha$ indicates the mass supply of liquid water if α represents water. By use of the identity described in (2.80) and substituting (2.82) into Eqn.(2.7), we have

$$\int_{\mathcal{V}_1^\alpha + \mathcal{V}_2^\alpha} \left[\frac{\partial \rho^\alpha}{\partial t} + \nabla \cdot (\rho^\alpha \mathbf{v}^\alpha) - \hat{\rho}^\alpha \right] \, dv + \int_{\Gamma(t)} [[\rho^\alpha \mathbf{u}_\Gamma^\alpha]] \cdot \mathbf{n} \, da = \int_{\Gamma(t)} \bar{\rho}^\alpha \, da \tag{2.84}$$

It is noticed that the term in the parenthesis on the left of Eqn.(2.84) is just the local form of the balance of mass for constituent α. Therefore we can get rid of the integral in the equation, and obtain the jump condition of mass in local form, as[3]

$$[[\rho^\alpha \mathbf{u}_\Gamma^\alpha]] \cdot \mathbf{n} = \bar{\rho}^\alpha \tag{2.85}$$

[3]The signs here are different with that given by Ateshian [17] for the jump condition of mass as well as other jump conditions because we are using an opposite direction for the unit normal $\mathbf{n}$.

The jump of mass for the mixture is then given by

$$[[\rho \mathbf{u}_\Gamma]] \cdot \mathbf{n} = 0 \tag{2.86}$$

where $\mathbf{u}_\Gamma$ is the diffusion velocity of the mixture relative to the singular surface defined by

$$\mathbf{u}_\Gamma = \mathbf{v} - \mathbf{v}_\Gamma \tag{2.87}$$

2.5.2 Jump of momentum

Like the balance of linear momentum for individual constituents, the linear momentum supply on the singular surface consists of two parts given by

$$\bar{\mathbf{s}}^\alpha = \bar{\rho}^\alpha \mathbf{v}^\alpha + \bar{\mathbf{p}}^\alpha \tag{2.88}$$

where the first part is the momentum gained by the mass supply, and the second is the momentum supply aside from chemical reaction or phase change. Moreover, similar to the mass supply $\bar{\rho}^\alpha$ on $\Gamma(t)$, the summation of $\bar{s}^\alpha$ over all constituents is zero, and so for all the surface supply terms in the following text. By use of (2.79), (2.80), and (2.88), Eqn.(2.19) becomes

$$\begin{aligned} \int_{\mathcal{V}_1^\alpha + \mathcal{V}_2^\alpha} \left[\frac{\partial(\rho^\alpha \mathbf{v}^\alpha)}{\partial t} + \nabla \cdot (\rho^\alpha \mathbf{v}^\alpha \otimes \mathbf{v}^\alpha) - \nabla \cdot \mathbf{T}^\alpha - \rho^\alpha \mathbf{b}^\alpha - \hat{\rho}^\alpha \mathbf{v}^\alpha - \hat{\mathbf{p}}^\alpha \right] dv \\ + \int_{\Gamma(t)} [[\rho^\alpha \mathbf{v}^\alpha \otimes \mathbf{u}_\Gamma^\alpha]] \cdot \mathbf{n} \, da = \int_{\Gamma(t)} [[\mathbf{T}^\alpha]] \cdot \mathbf{n} \, da + \int_{\Gamma(t)} \bar{\mathbf{s}}^\alpha \, da \end{aligned} \tag{2.89}$$

Using the local form of the balance of momentum for individual constituents, the first term on the left of the above equation is eliminated. We then obtain the jump condition of linear momentum expressed as

$$[[\rho^\alpha \mathbf{v}^\alpha \otimes \mathbf{u}_\Gamma^\alpha - \mathbf{T}^\alpha]] \cdot \mathbf{n} = \bar{\mathbf{s}}^\alpha \tag{2.90}$$

and the jump condition of linear momentum for the mixture is given by

$$[[\rho \mathbf{v} \otimes \mathbf{u}_\Gamma - \mathbf{T}]] \cdot \mathbf{n} = 0 \tag{2.91}$$

Likewise, the angular momentum by the local interaction for constituent α given in Eqn.(2.28) inside $\mathcal{V}$ containing a singular surface may be expanded to

$$\int_{\partial\mathcal{V}^\alpha} [\mathbf{x}\times(\hat{\mathbf{p}}^\alpha+\hat{\rho}^\alpha\mathbf{v}^\alpha)+\hat{\mathbf{m}}^\alpha] \;\; dv = \int_{\mathcal{V}_1^\alpha+\mathcal{V}_2^\alpha} [\mathbf{x}\times(\hat{\mathbf{p}}^\alpha+\hat{\rho}^\alpha\mathbf{v}^\alpha)+\hat{\mathbf{m}}^\alpha] \;\; dv + \int_{\Gamma(t)} (\mathbf{x}\times\bar{\mathbf{s}}^\alpha+\bar{\mathbf{n}}^\alpha)\; da \tag{2.92}$$

where $\bar{\mathbf{n}}^\alpha$ plays the same role as $\bar{\mathbf{s}}^\alpha$ in Eqn.(2.88). With (2.79), (2.80), and (2.92), Eqn.2.28) is expanded to

$$\begin{aligned}&\int_{\mathcal{V}_1^\alpha+\mathcal{V}_2^\alpha} [\mathbf{x}\times\mathbf{v}^\alpha(\frac{D^\alpha\rho^\alpha}{Dt}+\rho^\alpha\nabla\cdot\mathbf{v}^\alpha-\hat{\rho}^\alpha)+\mathbf{x}\times(\rho^\alpha\mathbf{a}^\alpha-\nabla\cdot\mathbf{T}^\alpha-\rho^\alpha\mathbf{b}^\alpha-\hat{\mathbf{p}}^\alpha)]\; dv\\ &-\int_{\mathcal{V}_1^\alpha+\mathcal{V}_2^\alpha}(\mathbf{g}^\alpha+\hat{\mathbf{m}}^\alpha)\; dv+\int_{\Gamma(t)} \mathbf{x}\times[[\rho^\alpha\mathbf{v}^\alpha\otimes\mathbf{u}_\Gamma^\alpha-\mathbf{T}^\alpha]]\cdot\mathbf{n}\; da=\int_{\Gamma(t)}(\mathbf{x}\times\bar{\mathbf{s}}^\alpha+\bar{\mathbf{n}}^\alpha)\; da\end{aligned} \tag{2.93}$$

By use of the local form of the balance of mass, the balance of linear momentum and the balance of angular momentum for constituent α, Eqn.(2.93) becomes

$$\mathbf{x}\times([[\rho^\alpha\mathbf{v}^\alpha\otimes\mathbf{u}_\Gamma^\alpha-\mathbf{T}^\alpha]]\cdot\mathbf{n}-\bar{\mathbf{s}}^\alpha)=\bar{\mathbf{n}}^\alpha \tag{2.94}$$

where the term in parenthesis in the left is just the jump condition of linear momentum for constituent α. Therefore once the jump of linear momentum is satisfied, we have

$$\bar{\mathbf{n}}^\alpha=0 \tag{2.95}$$

It is noticed that although the equations of jump of linear and angular momentum are not used for the vascular graft degradation problem, we want to show them here because they play important roles for problems with deformation or remodeling, which exist for most problems dealing with biological tissues. Therefore the jump conditions of momentum are extremely valuable for future research, and same for the jump of energy and entropy in the next section.

2.5.3 Jump of energy and entropy

The rate of energy supply on the singular surface is given by

$$\bar{w}^\alpha = \bar{\rho}^\alpha(\varepsilon^\alpha + \frac{1}{2}\mathbf{v}^\alpha \cdot \mathbf{v}^\alpha) + \bar{\mathbf{p}}^\alpha \cdot \mathbf{v}^\alpha + \bar{\varepsilon}^\alpha \tag{2.96}$$

where $\bar{\rho}^\alpha(\varepsilon^\alpha + \frac{1}{2}\mathbf{v}^\alpha \cdot \mathbf{v}^\alpha)$ is the rate of energy supply brought by mass supply; $\bar{\mathbf{p}}^\alpha \cdot \mathbf{v}^\alpha$ is the rate of energy supply from momentum supply; and $\bar{\varepsilon}^\alpha$ rate of energy transferred by contact. Again, by substituting (2.79) and (2.80) into Eqn.(2.43), we obtain the jump of energy for constituent α as

$$[[\rho^\alpha(\varepsilon^\alpha + \frac{1}{2}\mathbf{v}^\alpha \cdot \mathbf{v}^\alpha)\mathbf{u}_\Gamma^\alpha - (\mathbf{T}^\alpha)^{\mathrm{T}} \cdot \mathbf{v}^\alpha + \mathbf{q}^\alpha]] \cdot \mathbf{n} = \bar{w}^\alpha \tag{2.97}$$

and the jump condition of energy for the mixture is

$$[[\rho(\varepsilon + \frac{1}{2}\mathbf{v} \cdot \mathbf{v})\mathbf{u}_\Gamma - \mathbf{T}^{\mathrm{T}} \cdot \mathbf{v} + \mathbf{q}]] \cdot \mathbf{n} = 0 \tag{2.98}$$

Since the entropy inequality cannot be expressed strictly in local form, we only present the jump of entropy for the mixture here. With the understanding that $\sum_\alpha(\mathbf{h}^\alpha/\theta^\alpha) = \mathbf{h}/\theta$ and $\sum_\alpha(\rho^\alpha\gamma^\alpha/\theta^\alpha) = (\rho\gamma/\theta)$, by use of (2.79) and (2.80), the inequality (2.63) becomes

$$\int_{\mathcal{V}_1^\alpha + \mathcal{V}_2^\alpha} \left[\frac{\partial(\rho\eta)}{\partial t} + \nabla \cdot (\rho\eta\mathbf{v}) + \nabla \cdot (\frac{\mathbf{h}}{\theta}) - \frac{\rho\gamma}{\theta}\right] \, dv + \int_{\Gamma(t)} [[\rho\eta\mathbf{u}_\Gamma + \frac{\mathbf{h}}{\theta}]] \cdot \mathbf{n} \, da \geqslant 0 \tag{2.99}$$

Because (2.99) is valid for all shapes of $\mathcal{V}$, for a material region containing a singular surface shown in Figure 2, if we compress $\mathcal{V}_1$ and $\mathcal{V}_2$ and make the $\partial\mathcal{V}$ approach and infinitely close to $\Gamma(t)$, $\partial\mathcal{V}$ would coincide with $\Gamma(t)$ and the volume of the material region would be approximately zero. In this case, all properties inside ($\mathcal{V}_1$+$\mathcal{V}_2$) can be considered as zero. Therefore the first term in Eqn.(2.99) can be eliminated [33]. We then obtain the local form of the jump of entropy, as

$$[[\rho\eta\mathbf{u}_\Gamma + \frac{\mathbf{h}}{\theta}]] \cdot \mathbf{n} \geqslant 0 \tag{2.100}$$

3.0 GOVERNING EQUATIONS AND MOVING BOUNDARY CONDITIONS

Now let us formulate the governing equations and boundary conditions for the degradation problem of the vascular graft. Although there is no evidence showing that the degrading vascular graft is highly asymmetric, for a general standpoint, we postulate that *in vivo* it is possible that the shape of the graft could become irregular over time as shown in Figure 3. It is noticed that both the two boundaries of the vascular graft are changing with time. Also, if blood flow occurs inside the graft, there will also be a variation in the axial direction for the properties of the degrading graft. Therefore, this becomes a three dimensional unsteady problem. For convenience, the following equations are expressed in vector forms.

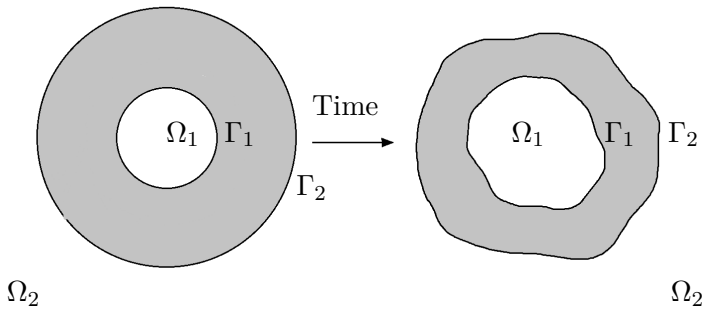


Figure 3: A cross section of an asymmetrically degrading biodegradable vascular graft over time. Γ_1 and Γ_2 represent the inner and the outer surfaces of the graft, respectively; Ω_1 represents the inner domain; Ω_2 represents the outer domain.

3.1 GOVERNING EQUATION

In the experiment by our group, the vascular grafts are made of a single degradable material such that only one solute need to be considered. Moreover, there is no chemical reaction between the solute and the solvent. Therefore if we apply the idea of mixture theory to this problem, there are overall three constituents that need to be considered: the solid s, the solute u, and the solvent w. For the solute u, the balance of mass is

$$\frac{D^u\rho^u}{Dt} + \rho^u \nabla \cdot \mathbf{v}^u = \hat{\rho}^u \qquad \text{in } \Omega_1,\ \Omega_2 \tag{3.1}$$

Since there is no chemical reaction or phase transition, by expanding the first term, Eqn.(3.1) becomes

$$\frac{\partial \rho^u}{\partial t} + \mathbf{v}^u \cdot \nabla \rho^u + \rho^u \nabla \cdot \mathbf{v}^u = \frac{\partial \rho^u}{\partial t} + \nabla \cdot (\rho^u \mathbf{v}^u) = 0 \qquad \text{in } \Omega_1,\ \Omega_2 \tag{3.2}$$

According to Fick's law, the mass flux for the solute u is

$$\mathbf{F} = -\mathbf{D}\nabla C = C(\mathbf{v}^u - \mathbf{v}^w) \qquad \text{in } \Omega_1,\ \Omega_2 \tag{3.3}$$

where C represents the concentration of u, which is also the apparent density of the solute. By substituting the divergence of (3.3) into Eqn.(3.2), with the understanding that $\nabla \cdot \mathbf{v}^w = 0$[4] for an incompressible fluid, we obtain

$$\frac{\partial C}{\partial t} + \mathbf{v}^w \cdot \nabla C = \nabla \cdot (\mathbf{D}\nabla C) \qquad \text{in } \Omega_1,\ \Omega_2 \tag{3.4}$$

and this is the general governing equation for the degradation process.

3.2 THE MOVING BOUNDARIES

As will be discussed below, the inner surface and the outer surface of the degrading graft are both dependent on time, and two boundary conditions are required for each boundary to constrain

[4] $\mathbf{v}^w = \mathbf{v}$ since the velocity of the mixture for the solution is the velocity of the solvent.

the time dependent boundary. If $\mathbf{n}$ is defined as the unit normal that points into the solution side on the interfaces between the solid and the solution, according to Noyes-Whitney constitutive equation [26], which suggests that the mass supply rate at the boundary is proportional to the difference between concentration C at time t and the saturation solubility C_s, the first boundary condition is given by

$$-\mathbf{D}\nabla C \cdot \mathbf{n} = h(C_s - C) \qquad \text{at } \Gamma_1,\ \Gamma_2 \tag{3.5}$$

This is the Robin boundary condition that suggests that the mass flux at the boundary is proportional to the difference between concentration C at time t and the saturation solubility C_s, where h is a material coefficient.

The second boundary condition arises in this problem because of the moving boundary. Conventionally, we call boundary conditions of this type the moving boundary conditions or Stefan boundary conditions. Although the graft is highly porous, Gade *et al.* [34] showed that it lost mass mainly by surface erosion and the apparent density barely changes. Therefore the effect of porosity is ignored in deriving the moving boundary conditions. We denote the properties in the solution with asterisk to distinguish them from the properties of the solid. At the surfaces of the graft, by use of the jump condition given in Eqn.(2.85), for constituent s, we have

$$\rho^s_*(\mathbf{v}^s_* - \mathbf{v}_\Gamma) \cdot \mathbf{n} - \rho^s(\mathbf{v}^s - \mathbf{v}_\Gamma) \cdot \mathbf{n} = \bar{\rho}^s \qquad \text{at } \Gamma_1,\ \Gamma_2 \tag{3.6}$$

Since there is no solid in the solution, we have $\rho^s_* = 0$. Moreover, if the graft is assumed to be fixed in the space, $\mathbf{v}^s$ is zero. Thus (3.6) is reduced to

$$\rho^s \mathbf{v}_\Gamma \cdot \mathbf{n} = \bar{\rho}^s \qquad \text{at } \Gamma_1,\ \Gamma_2 \tag{3.7}$$

Again, by Noyes-Whitney constitutive equation, we have

$$\bar{\rho}^s = -h(C_s - C) \qquad \text{at } \Gamma_1,\ \Gamma_2 \tag{3.8}$$

where the negative sign implies that the mass supply to solid s is negative.

By use of (3.5), (3.7), and (3.8), the moving boundary condition is obtained as

$$\rho^s \mathbf{v}_\Gamma \cdot \mathbf{n} = \mathbf{D}\nabla C \cdot \mathbf{n} \qquad \text{at } \Gamma_1,\ \Gamma_2 \tag{3.9}$$

4.0 MATHEMATICAL MODEL FOR THE *IN VITRO* DEGRADATION OF THE VASCULAR GRAFT

In this chapter, we developed a mathematical model for the *in vitro* degradation problem, which considers a vascular graft degrading in stationary solution. The purpose for this study is to understand the effect of degradation and extend the results to the *in vivo* problem which can not be studied directly. The experiment related to this thesis has been conducted by our group. In particular, Gade *et al.* [34] tested the effect of enzymatic degradation for vascular grafts made of fast degrading poly (glycerol sebacate) (PGS) in a stationary solution. It was found that the mass loss of the *in vitro* degradation can be predicted through two degradation constants h and D, which enables the prediction of the *in vivo* mass loss by tuning the two constants. It should be noticed cellular attachment and growth are not included for the problem in this chapter.

4.1 MATHEMATICAL MODEL

For the *in vitro* problem, it is reasonable to assume that the degradation is independent of axial direction since there is no blood flow inside the inner domain. Also, we assume that the graft remains axisymmetric over time. Thus the original problem is reduced to a one-dimensional problems as shown in Figure 4, where the outside boundary Γ_3 is an analogy to the wall of the container in the experiment, at which

$$\mathbf{D}\nabla C \cdot \mathbf{n} = 0 \qquad \text{in } \Omega_1,\ \Omega_2 \tag{4.1}$$

Also, radiuses of the moving boundaries R_1 and R_2 only depend on time. We have

$$\mathbf{v}_{\Gamma_i} \cdot \mathbf{n} = -\frac{dR_i(t)}{dt} \qquad i = 1,\ 2 \text{ at } \Gamma_1,\ \Gamma_2 \tag{4.2}$$

By substituting (4.2) into the moving boundary condition (3.9), we obtain

$$-\rho^s \frac{dR_i(t)}{dt} = \mathbf{D}\nabla C \cdot \mathbf{n} \qquad i = 1,\ 2 \text{ at } \Gamma_1,\ \Gamma_2 \tag{4.3}$$

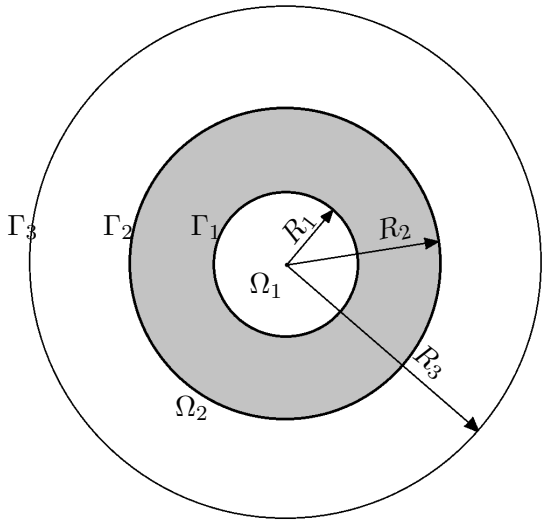


Figure 4: A cross section of the vascular graft. Γ_1 and Γ_2 represent the inner and the outer surfaces of the graft, respectively; Γ_3 is the outer boundary; Ω_1 represents the inner domain; Ω_2 represents the outer domain.

We idealize the diffusion coefficient D is uniform and independent of C, and axial diffusion is neglected. For the solute, although there are velocities in radial direction near the two moving boundaries, we can assume that the solute is stationary since the motions of the two surfaces are slow enough, which implies that $\mathbf{v}^w = 0$. Thus in cylinder coordinate, the governing equation given in (3.4) is written as

$$\frac{\partial C}{\partial t} = D\frac{1}{r}\frac{\partial}{\partial r}(r\frac{\partial C}{\partial r}) \qquad \text{in } \Omega_1,\ \Omega_2 \tag{4.4}$$

By using the boundary conditions given in (3.5) and (4.3), if we set the initial concentration to be zero, for the inner domain Ω_1, the equation set for $C(r,t)$ is

$$\frac{\partial C}{\partial t} = D\frac{1}{r}\frac{\partial}{\partial r}(r\frac{\partial C}{\partial r}) \qquad 0 < r < R_1(t),\ t > 0 \tag{4.5}$$

$$\rho_s \frac{dR_1(t)}{dt} = D\frac{\partial C}{\partial r} \qquad r = R_1(t),\ t > 0 \tag{4.6}$$

$$D\frac{\partial C}{\partial r} = h(C_s - C) \qquad r = R_1(t),\ t > 0 \tag{4.7}$$

$$C(r,0) = 0 \qquad 0 < r < R_1(t),\ t = 0 \tag{4.8}$$

$$R_1(0) = R_1^0 \qquad t = 0 \tag{4.9}$$

where R_1^0 denotes the initial value of R_1.

Likewise, for the outer domain Ω_2, with boundary conditions (3.5), (4.1), and (4.3), the equation set for $C(r,t)$ is

$$\frac{\partial C}{\partial t} = D\frac{1}{r}\frac{\partial}{\partial r}(r\frac{\partial C}{\partial r}) \qquad R_2(t) < r < R_3,\ t > 0 \tag{4.10}$$

$$\rho_s \frac{dR_1(t)}{dt} = D\frac{\partial C}{\partial r} \qquad r = R_2(t),\ t > 0 \tag{4.11}$$

$$-D\frac{\partial C}{\partial r} = h(C_s - C) \qquad r = R_2(t),\ t > 0 \tag{4.12}$$

$$\frac{\partial C}{\partial r} = 0 \qquad r = R_3,\ t > 0 \tag{4.13}$$

$$C(r,0) = 0 \qquad R_2(t) < r < R_3,\ t = 0 \tag{4.14}$$

$$R_2(0) = R_2^0 \qquad t = 0 \tag{4.15}$$

where R_2^0 denotes the initial value of R_2.

4.2 SOLUTION TO THE *IN VITRO* PROBLEM

For the linear partial differential given in Eqn.(4.4), the moving boundary condition introduce extra non-linearity into the problem [25]. Even though for some moving boundary problems with infinite domain or semi-infinite domain, it is possible to find their closed form solutions in the form of error functions by use of change of a variable, a solution in closed form may not exist for most moving boundary problems with a finite domain. As a result, for this degradation problem with

a finite domain, an approximate method have to be introduced. In this section, we will find the approximate solution with the aid of regular perturbation theory.

4.2.1 Solution for the inner domain

The following dimensionless properties and parameters are introduced.

$$\bar{C} = \frac{C_s - C}{C_s} \qquad \zeta = \frac{r}{R_1(t)} \qquad \tau = \frac{Dt}{R_1^{0\,2}}$$
$$\bar{R} = \frac{R_1(t)}{R_1^0} \qquad \epsilon = \frac{C_s}{\rho_s} \qquad \beta = \frac{hR_1^0}{D} \tag{4.16}$$

With these expressions, the non-dimensional form of (4.5)-(4.9) is written as

$$\bar{R}^2 \frac{\partial \bar{C}}{\partial \tau} + \epsilon\zeta \left.\frac{\partial \bar{C}}{\partial \zeta}\right|_{\zeta=1} \frac{\partial \bar{C}}{\partial \zeta} = \frac{\partial^2 \bar{C}}{\partial \zeta^2} + \frac{1}{\zeta}\frac{\partial \bar{C}}{\partial \zeta} \qquad 0 < \zeta < 1, \quad \tau > 0 \tag{4.17}$$

$$\frac{\partial \bar{C}}{\partial \zeta} = -\beta \bar{R} \bar{C} \qquad \zeta = 1, \quad \tau > 0 \tag{4.18}$$

$$\bar{R}\frac{d\bar{R}}{d\tau} = -\epsilon \frac{\partial \bar{C}}{\partial \zeta} \qquad \zeta = 1, \quad \tau > 0 \tag{4.19}$$

$$\bar{C} = 1 \qquad 0 < \zeta < 1, \quad \tau = 0 \tag{4.20}$$

$$\bar{R} = 1 \qquad \tau = 0 \tag{4.21}$$

Thus in addition to rewriting the problem in a non-dimensional form, the inner domain with a moving boundary is mapped to a fixed domain by non-dimensionalization.

In the experiment by Gade *et al.* [34], the value of the dimensionless parameter ϵ is small with a magnitude of 10^{-4}. As a result, ϵ is identified as the small parameter[5] required by perturbation theory. Thus we may expand $\bar{C}$ and $\bar{R}$ to

$$\bar{C} = \bar{C}_0 + \epsilon\bar{C}_1 + \epsilon^2\bar{C}_2 + \cdots = \sum_n \epsilon^n \bar{C}_n \tag{4.22}$$

$$\bar{R} = \bar{R}_0 + \epsilon\bar{R}_1 + \epsilon^2\bar{R}_2 + \cdots = \sum_n \epsilon^n \bar{R}_n \tag{4.23}$$

[5]For regular perturbation theory, ϵ is not necessarily to be a small number. In fact, there is a non-vanishing radius of convergence. That is to say, the series solution obtained by regular perturbation theory is convergent even for very large ϵ. We want ϵ to be small here because we can get the accurate approximate solution by only solving first few order problems, otherwise we have to calculate high order solutions to obtain a satisfactory result if ϵ is large. Sometimes if there is no such a small parameter, we can just introduce a parameter into the problem and let $\epsilon = 1$ to recover the original problem after calculation [35].

where $\bar{C}_n$ and $\bar{R}_n$ represents the n^{th} order solution of $\bar{C}$ and $\bar{R}$, respectively. By substituting (4.22) and (4.23) into the moving boundary condition (4.19) and rearranging terms, we get

$$\bar{R}_0\frac{d\bar{R}_0}{d\tau} + (\bar{R}_0\frac{d\bar{R}_1}{d\tau} + \bar{R}_1\frac{d\bar{R}_0}{d\tau} + \left.\frac{\partial\bar{C}_0}{\partial\zeta}\right|_{\zeta=1})\varepsilon + (\bar{R}_0\frac{d\bar{R}_2}{d\tau} + \bar{R}_1\frac{d\bar{R}_1}{d\tau} + \bar{R}_2\frac{d\bar{R}_0}{d\tau} + \left.\frac{\partial\bar{C}_1}{\partial\zeta}\right|_{\zeta=1})\varepsilon^2 + \cdots = 0 \tag{4.24}$$

Since Taylor expansion is unique for any convergent series, we may let every coefficients of ε^n in Eqn.(4.24) to be zero, and get

$$\bar{R}_0\frac{d\bar{R}_0}{d\tau} = 0 \tag{4.25}$$

$$\bar{R}_0\frac{d\bar{R}_1}{d\tau} + \bar{R}_1\frac{d\bar{R}_0}{d\tau} = -\left.\frac{\partial\bar{C}_0}{\partial\zeta}\right|_{\zeta=1} \tag{4.26}$$

$$\bar{R}_0\frac{d\bar{R}_2}{d\tau} + \bar{R}_1\frac{d\bar{R}_1}{d\tau} + \bar{R}_2\frac{d\bar{R}_0}{d\tau} = -\left.\frac{\partial\bar{C}_1}{\partial\zeta}\right|_{\zeta=1} \tag{4.27}$$

$$\vdots$$

Similarly, Eqn.(4.17) is expanded with the understating that $\bar{R}_0$ is constant. Again, we let the coefficients of ϵ^n to be zero, and obtain

$$\bar{R}_0^2\frac{\partial\bar{C}_0}{\partial\tau} = \frac{\partial^2\bar{C}_0}{\partial\zeta^2} + \frac{1}{\zeta}\frac{\partial\bar{C}_0}{\partial\zeta} \tag{4.28}$$

$$\bar{R}_0^2\frac{\partial\bar{C}_1}{\partial\tau} + 2\bar{R}_0\bar{R}_1\frac{\partial\bar{C}_0}{\partial\tau} - \zeta\frac{d\bar{R}_1}{d\tau}\frac{\partial\bar{C}_0}{\partial\zeta} = \frac{\partial^2\bar{C}_1}{\partial\zeta^2} + \frac{1}{\zeta}\frac{\partial\bar{C}_1}{\partial\zeta} \tag{4.29}$$

$$\vdots$$

$$\bar{R}_0^2\frac{\partial\bar{C}_n}{\partial\tau} + F(\zeta,\tau) = \frac{\partial^2\bar{C}_n}{\partial\zeta^2} + \frac{1}{\zeta}\frac{\partial\bar{C}_n}{\partial\zeta} \tag{4.30}$$

where

$$F(\zeta,\tau) = 2\sum_{i=0}^{[\frac{n-1}{2}]}\sum_{j=i+1}^{n-i}\bar{R}_i\bar{R}_j\frac{\partial\bar{C}_{n-i-j}}{\partial\tau} + \sum_{i=1}^{[\frac{n}{2}]}\bar{R}_i^2\frac{\partial\bar{C}_{n-2i}}{\partial\tau} - \zeta\sum_{i=0}^{n-1}\sum_{j=1}^{n-i}R_i\frac{d\bar{R}_j}{d\tau}\frac{\partial\bar{C}_{n-i-j}}{\partial\zeta} \tag{4.31}$$

The parenthesis operation in (4.31) represents the function that round the number to the lower integer. Moreover, the Robin boundary condition and the initial conditions of $\bar{C}$ and $\bar{R}$ imply that

$$\frac{\partial \bar{C}_n}{\partial \zeta} = -\beta \sum_{i=0}^{n} \bar{R}_i \bar{C}_{n-i} \qquad \zeta = 1,\ \tau > 0 \tag{4.32}$$

$$\bar{R}_0 = 1,\ \bar{R}_n(0) = 0 \tag{4.33}$$

$$\bar{C}_0(0) = 1,\ \bar{C}_n(0) = 0 \tag{4.34}$$

Therefore the moving boundary problem is reduced to infinite boundary value problems in a fixed domain. In addition, we notice that the inhomogeneous term F for problems in which $n \geqslant 1$ is known as long as the lower order solutions of $\bar{C}_n$ and $\bar{R}_n$ are obtained. Such that theoretically the problem can be solved recursively. The equation set for the 0^{th} order problem[6] is

$$\frac{\partial \bar{C}_0}{\partial \tau} = \frac{\partial^2 \bar{C}_0}{\partial \zeta^2} + \frac{1}{\zeta}\frac{\partial \bar{C}_0}{\partial \zeta} \qquad 0 < \zeta < 1, \quad \tau > 0 \tag{4.35}$$

$$\frac{\partial \bar{C}_0}{\partial \zeta} = -\beta \bar{C}_0 \qquad \zeta = 1, \quad \tau > 0 \tag{4.36}$$

$$\bar{C}_0 = 1 \qquad 0 < \zeta < 1,\ \tau = 0 \tag{4.37}$$

$$\bar{R}_0 = 1 \qquad \tau \geq 0 \tag{4.38}$$

It can be seen that this 0^{th} order problem is the simplification of the original problem under the quasi-stationary assumption. By applying separation of variables, the solution is shown to be

$$\bar{C}_0 = \sum_{n=1}^{\infty} \frac{2\beta J_0(\alpha_n \zeta)}{(\alpha_n^2 + \beta^2) J_0(\alpha_n)} e^{-{\alpha_n}^2 \tau} \tag{4.39}$$

where α_n are the roots of the eigenfunction

$$\alpha_n J_1(\alpha_n) = \beta J_0(\alpha_n) \tag{4.40}$$

and J_0 is the Bessel function of the first kind of 0^{th} order; J_1 is the Bessel function of the first kind of first order. Therefore the 0^{th} order solution $\bar{C}_0$ is obtained. Next, let us recall the relationship between $\bar{C}_0$ and $\bar{R}_1$ described by (4.26). By substituting the zero$^{\text{th}}$ order solution of the concen-

[6] 0^{th} order problem is also called unperturbed problem. It can be obtained just by letting $\epsilon = 0$.

tration into Eqn.(4.26), the first order solution of the non-dimensional inner radius $\bar{R}_1$ is obtained as

$$\bar{R}_1 = \sum_{n=1}^{\infty} \frac{2\beta^2}{(\alpha_n^2 + \beta^2)\alpha_n^2}(1 - e^{-{\alpha_n}^2\tau}) \tag{4.41}$$

However, the first order problem for $\bar{C}_1$ is difficult to solve analytically because $\bar{C}_0$ and $\bar{R}_1$ are infinite-series. Fortunately, the accuracy of the first order solution of $\bar{R}$ is satisfactory and we will prove it using numerical methods in the next chapter. Consequently, the approximate solution for the radius of the inner domain with first order accuracy is

$$\bar{R} = \bar{R}_0 + \varepsilon\bar{R}_1 = 1 + \varepsilon \sum_{n=1}^{\infty} \frac{2\beta^2}{(\alpha_n^2 + \beta^2)\alpha_n^2}(1 - e^{-{\alpha_n}^2\tau}) \tag{4.42}$$

and therefore the mass loss per unit length for the inner domain is

$$\Delta m = 2\pi R_1 \int_0^t h(C_s - C)\, dt = \sum_{n=1}^{\infty} \frac{4\pi(R_1^0)^2\bar{R}\beta^2 C_s}{({\alpha_n}^2 + \beta^2){\alpha_n}^2}(1 - e^{-{\alpha_n}^2\tau}) \tag{4.43}$$

One interesting feature is that, if we substitute the solution of $\bar{C}_0$ into the moving boundary condition (4.19) and integrate both sides with respect to τ, the same result as shown in Eqn.(4.42) may also be obtained.

4.2.2 Solution for the outer domain

Likewise, we mapped the time dependent domain into a fixed domain by non-dimensionalization. The dimensionless properties and parameters are described as follows.

$$\begin{aligned} &\bar{C} = \frac{C_s - C}{C_s} \qquad \zeta = \frac{r - R_2(t)}{R_3 - R_2(t)} \qquad \tau = \frac{Dt}{(R_3 - R_2^0)^2} \qquad \bar{R} = \frac{R_3 - R_2(t)}{R_3 - R_2^0} \\ &\epsilon = \frac{C_s}{\rho_s} \qquad \beta = \frac{h(R_3 - R_2^0)}{D} \qquad \bar{a} = \frac{R_2^0}{R_3 - R_2^0} \qquad R_c = \frac{R_2(t)}{R_3 - R_2(t)} \end{aligned} \tag{4.44}$$

where R_2^0 represents the initial value of R_2. Accordingly, the normalized problem is

$$\bar{R}^2\frac{\partial \bar{C}}{\partial \tau} - \epsilon(\zeta-1)\left.\frac{\partial \bar{C}}{\partial \zeta}\right|_{\zeta=0}\frac{\partial \bar{C}}{\partial \zeta} = \frac{\partial^2 \bar{C}}{\partial \zeta^2} + \frac{1}{\zeta + R_c}\frac{\partial \bar{C}}{\partial \zeta} \qquad 0<\zeta<1, \quad \tau>0 \tag{4.45}$$

$$\frac{\partial \bar{C}}{\partial \zeta} = \beta \bar{R}\bar{C} \qquad \zeta = 0, \quad \tau > 0 \tag{4.46}$$

$$\bar{R}\frac{d\bar{R}}{d\tau} = \epsilon\frac{\partial \bar{C}}{\partial \zeta} \qquad \zeta = 0, \quad \tau > 0 \tag{4.47}$$

$$\frac{\partial \bar{C}}{\partial \zeta} = 0 \qquad \zeta = 1, \quad \tau > 0 \tag{4.48}$$

$$\bar{C} = 1 \qquad 0<\zeta<1, \quad \tau = 0 \tag{4.49}$$

$$\bar{R} = 1 \qquad \tau = 0 \tag{4.50}$$

By letting $\epsilon = 0$, we obtain the 0^{th} order problem which is written as

$$\frac{\partial \bar{C}_0}{\partial \tau} = \frac{\partial^2 \bar{C}_0}{\partial \zeta^2} + \frac{1}{\zeta + \bar{a}}\frac{\partial \bar{C}_0}{\partial \zeta} \qquad 0<\zeta<1, \ \tau>0 \tag{4.51}$$

$$\frac{\partial \bar{C}_0}{\partial \zeta} = \beta \bar{C}_0 \qquad \zeta = 0, \ \tau > 0 \tag{4.52}$$

$$\frac{\partial \bar{C}_0}{\partial \zeta} = 0 \qquad \zeta = 1, \ \tau > 0 \tag{4.53}$$

$$\bar{C}_0 = 1 \qquad 0<\zeta<1, \ \tau = 0 \tag{4.54}$$

Likewise, with the aid of separation of variables, the solution to this problem is

$$\bar{C}_0 = \sum_{n=1}^{\infty} D_n \phi[\alpha_n(\zeta + \bar{a})]e^{-\alpha_n^2 \tau} \tag{4.55}$$

where

$$\phi[\alpha_n(\zeta+\bar{a})] = Y_1(\alpha_n\bar{a}+\alpha_n)J_0[\alpha_n(\zeta+\bar{a})] - J_1(\alpha_n\bar{a}+\alpha_n)Y_0[\alpha_n(\zeta+\bar{a})] \tag{4.56}$$

and α_n are eigenvalues of the eigenfunction

$$Y_1(\alpha_n\bar{a}+\alpha_n)J_0(\alpha_n\bar{a})-J_1(\alpha_n\bar{a}+\alpha_n)Y_0(\alpha_n\bar{a})=\alpha_nY_1(\alpha_n\bar{a})J_1[\alpha_n\bar{a}+\alpha_n]-\alpha_nJ_1(\alpha_n\bar{a})Y_1[\alpha_n\bar{a}+\alpha_n] \tag{4.57}$$

which is obtained from boundary condition (4.46).

The coefficient D_n is given by

$$D_n=\frac{2\bar{a}\beta\phi(\bar{a}\alpha_n)}{(1+\bar{a})^2{\alpha_n}^2\phi^2[\alpha_n(1+\bar{a})]-\bar{a}^2(\beta^2+{\alpha_n}^2)\phi^2(\alpha_n\bar{a})} \tag{4.58}$$

With the 0^{th} order solution of concentration, the approximate solution of $\bar{R}$ with first order accuracy may be obtained as

$$\bar{R}=1+\varepsilon\sum_{n=1}^{\infty}\frac{\beta D_n\phi(\bar{a}\alpha_n)}{\alpha_n^2}(1-e^{-{\alpha_n}^2\tau}) \tag{4.59}$$

and the mass loss per unit length for the outer domain is

$$\begin{aligned}\Delta m&=2\pi R_2\int_0^t h(C_s-C)\,dt\\&=\sum_{n=1}^{\infty}\frac{2\pi C_s\beta[R_3-\bar{R}(R_3-R_2^0)](R_3-R_2^0)D_n\phi(\bar{a}\alpha_n)}{{\alpha_n}^2}(1-e^{-{\alpha_n}^2\tau})\end{aligned} \tag{4.60}$$

5.0 NUMERICAL SOLUTIONS FOR THE *IN VITRO* PROBLEM

In order to test the solutions we obtained in the previous chapter, we will now analyze the moving boundary problem numerically and compare the results to the approximate solutions.

5.1 NUMERICAL ANALYSIS FOR THE INNER DOMAIN

For convenience, we use R and C to represent the normalized and mapped inner radius $\bar{R}$ and the normalized concentration $\bar{C}$, respectively. We notice that although the inner radius of the graft is a function of time, the domain of the normalized problem remains fixed in time, which allows that the grid size and position are independent of time. As a result, implicit finite difference method can be applied here.

For the numerical approach, the first and second order derivatives with respect to ζ in Eqn.(4.17) are represented by central difference approximations as

$$\frac{\partial^2 C}{\partial \zeta^2} = \frac{C_{i+1} - 2C_i + C_{i-1}}{\Delta \zeta^2}, \ \frac{\partial C}{\partial \zeta} = \frac{C_{i+1} - C_{i-1}}{2\Delta \zeta} \qquad i = 0,\ 1,\ 2,\ 3,\ \cdots\ N \tag{5.1}$$

where C_i is the dimensionless concentration at the ith grid and $\Delta\zeta$ is the grid size. The time derivative term is approximated by a forward difference in time which is written as

$$\frac{\partial C}{\partial \tau} = \frac{C_i^{n+1} - C_i^n}{\Delta \tau} \qquad n = 0,\ 1,\ 2,\ 3,\ \cdots \tag{5.2}$$

where n represents the time level and $\Delta\tau$ is the time step. Now with these finite difference forms, (4.17)-(4.21) which describe the *in vitro* degradation of the vascular graft from the inner side become

$$(R^{n+1})^2\frac{C_i^{n+1}-C_i^n}{\Delta\tau}-i\Delta\zeta\epsilon\beta R^{n+1}C_N^{n+1}\frac{C_{i+1}^{n+1}-C_{i-1}^{n+1}}{\Delta\zeta}=$$
$$\frac{C_{i+1}^{n+1}-2C_i^{n+1}+C_{i-1}^{n+1}}{\Delta\zeta^2}+\frac{1}{i\Delta\zeta}\frac{C_{i+1}^{n+1}-C_{i-1}^{n+1}}{2\Delta\zeta}\qquad i=1,\ 2,\ 3,\ \cdots\ N-1 \tag{5.3}$$

$$\frac{C_{N+1}^{n+1}-C_{N-1}^{n+1}}{2\Delta\zeta}=-\beta R^{n+1}C_N^{n+1} \tag{5.4}$$

$$\frac{R^{n+1}-R^n}{\Delta\tau}=\epsilon\beta C_N^{n+1} \tag{5.5}$$

$$C_i^0=1\qquad i=0,\ 1,\ 2,\ 3,\ \cdots\ N \tag{5.6}$$

$$R^0=1 \tag{5.7}$$

It is noticed that $(N+1)$ is a ghost point on which the values are constrained by the boundary condition (5.4). Since the model is axisymmetric, the difference equation at $i=0$ is given by

$$(R^{n+1})^2\frac{C_0^{n+1}-C_0^n}{\Delta\tau}=4\frac{C_1^{n+1}-C_0^{n+1}}{\Delta\zeta^2} \tag{5.8}$$

By algebra operations, Eqn.(5.3) can be written as

$$\underbrace{\frac{a+2c}{a}}_{A_i^*}C_i^{n+1}+\underbrace{\frac{b-c-d}{a}}_{B_i^*}C_{i+1}^{n+1}+\underbrace{\frac{d-c-b}{a}}_{C_i^*}C_{i-1}^{n+1}=C_i^n\qquad i=1,\ 2,\ 3,\ \cdots\ N-1 \tag{5.9}$$

where

$$a=\frac{\left(R^{n+1}\right)^2}{\Delta\tau}\qquad b=\frac{-\epsilon\zeta\beta R^{n+1}C_N^{n+1}}{2\Delta\zeta}\qquad c=\frac{1}{\Delta\zeta^2}\qquad d=\frac{1}{2i\Delta\zeta^2} \tag{5.10}$$

Thus if we use $\mathbf{C}^{n+1}$ and $\mathbf{C}^n$ to represent the collection of concentrations at time $(n+1)$ and time n, respectively, the finite difference equation can be expressed in the following linear system.

$$\mathbf{E}\mathbf{C}^{n+1}=\mathbf{C}^n \tag{5.11}$$

where the matrix $\mathbf{E}$ is

$$\mathbf{E} = \begin{bmatrix} A_0^* & B_0^* & & & \\ C_1^* & A_1^* & B_1^* & & \\ & \ddots & \ddots & \ddots & \\ & & & C_N^* & A_N^* \end{bmatrix} \tag{5.12}$$

and

$$A_0^* = 1 + \frac{4}{a\Delta\zeta^2} \qquad B_0^* = -\frac{4}{a\Delta\zeta^2} \qquad C_N^* = \frac{-2c}{a} \qquad A_N^* = \frac{a+b+2c}{a} - 2\Delta\zeta\beta R^{n+1}\frac{b-c-d}{a} \tag{5.13}$$

At every time point n, the non-dimensional radius at the next time (n+1) denoted by R^{n+1} is assumed, and the concentration at $(n+1)$ can be obtained by Eqn.(5.11); next, R^{n+1} is updated using the moving boundary condition in (5.5); then the process is repeated until the iterated R^{n+1} does not change significantly, and we may go to the next time point.

In order to make the implicit finite difference method valid, convergence of the scheme is tested [36]. The Taylor expansions of C_i^{n+1}, $C_{i\pm1}^n$, and R^{n+1} are

$$C_i^{n+1} = C_i^n + \left(\frac{\partial C}{\partial \tau}\right)\Big|_i^n \Delta\tau + \left(\frac{\partial^2 C}{\partial \tau^2}\right)\Big|_i^n \frac{(\Delta\tau)^2}{2} + \cdots \tag{5.14}$$

$$C_{i\pm1}^n = C_i^n \pm \left(\frac{\partial C}{\partial \zeta}\right)\Big|_i^n \Delta\zeta + \left(\frac{\partial^2 C}{\partial \zeta^2}\right)\Big|_i^n \frac{(\Delta\zeta)^2}{2} \pm \cdots \tag{5.15}$$

$$R^{n+1} = R^n + \left(\frac{\partial R}{\partial \tau}\right)\Big|^n \Delta\tau + \left(\frac{\partial^2 R}{\partial \tau^2}\right)\Big|^n \frac{(\Delta\tau)^2}{2} + \cdots \tag{5.16}$$

Substituting (5.14)-(5.16) into the difference equation (5.3), we have

$$\bar{R}^2\frac{\partial \bar{C}}{\partial \tau} + \epsilon\zeta \left.\frac{\partial \bar{C}}{\partial \zeta}\right|_{\zeta=1} \frac{\partial \bar{C}}{\partial \zeta} = \frac{\partial^2 \bar{C}}{\partial \zeta^2} + \frac{1}{\zeta}\frac{\partial \bar{C}}{\partial \zeta} + O(\Delta\tau,\ \Delta\zeta^2) \tag{5.17}$$

As $\Delta\tau$ and $\Delta\zeta$ approach zero, Eqn.(5.17) is reduced to the original PDE as given in Eqn.(4.17). Therefore we say that this method is consistent and has the order of errors in $\Delta\tau$ and $\Delta\zeta^2$. Furthermore, because an implicit method is used for the finite difference method and there is no negative diffusion, the approach is unconditionally stable. Therefore according to Lax equivalence theorem [37], the consistency and stability imply that this numerical scheme is convergent.

5.2 NUMERICAL ANALYSIS FOR THE OUTER DOMAIN

It is noticed that an additional convection term appears as a result of mapping for the partial differential equations for both the inner domain and the outer domain. For the outer domain, the additional convection term may generate a negative numerical diffusion if central difference is applied, which can make the method unstable. As a result, the upwind method is applied to the convection term in Eqn.(4.45), which is defined by

$$\frac{\partial C}{\partial \zeta} = \frac{C_i - C_{i-1}}{\Delta \zeta} \qquad i = 0,\ 1,\ 2,\ 3,\ \cdots\ N \tag{5.18}$$

Therefore the finite difference forms of Eqn.(4.45)-(4.50) are given by

$$(R^{n+1})^2 \frac{C_i^{n+1} - C_i^n}{\Delta \tau} - (i\Delta\zeta - 1)\epsilon\beta R^{n+1} C_0^{n+1} \frac{C_i^{n+1} - C_{i-1}^{n+1}}{\Delta \zeta} =$$
$$\frac{C_{i+1}^{n+1} - 2C_i^{n+1} + C_{i-1}^{n+1}}{\Delta \zeta^2} + \frac{1}{i\Delta\zeta + R_c^{n+1}} \frac{C_{i+1}^{n+1} - C_{i-1}^{n+1}}{2\Delta\zeta} \qquad i = 1,\ 2,\ 3,\ \cdots\ N-1 \tag{5.19}$$

$$\frac{C_1^{n+1} - C_{-1}^{n+1}}{2\Delta\zeta} = \beta R^{n+1} C_0^{n+1} \tag{5.20}$$

$$\frac{R^{n+1} - R^n}{\Delta\tau} = \epsilon\beta C_0^n \tag{5.21}$$

$$C_i^0 = 1 \qquad i = 0,\ 1,\ 2,\ 3,\ \cdots\ N \tag{5.22}$$

$$R^0 = 1 \tag{5.23}$$

where C_{-1} is the concentration at the ghost point $i = -1$. Likewise, we may express Eqn.(5.19) in the following form, as

$$\underbrace{\frac{a+b+2c}{a}}_{A_i^*} C_i^{n+1} + \underbrace{\frac{-c-d}{a}}_{B_i^*} C_{i+1}^{n+1} + \underbrace{\frac{d-c-b}{a}}_{C_i^*} C_{i-1}^{n+1} = C_i^n \qquad i = 1,\ 2,\ 3,\ \cdots\ N-1 \tag{5.24}$$

where for the outer domain,

$$a = \frac{(R^{n+1})^2}{\Delta\tau} \qquad b = \frac{\epsilon(1 - i\zeta)\beta R^{n+1} C_0^{n+1}}{\Delta\zeta} \qquad c = \frac{1}{\Delta\zeta^2} \qquad d = \frac{1}{2\zeta(i\Delta\zeta + R_c^{n+1})} \tag{5.25}$$

Again, we can use the linear system given in Eqn.(5.11) to describe the problem. For the problem of the outer domain, we have

$$A_0^* = \frac{a+b+2c}{a} - 2\Delta\zeta\beta R^{n+1}\frac{d-c-b}{a} \qquad B_0^* = \frac{-2c-b}{a} \qquad C_N^* = \frac{-2c-b}{a} \qquad A_N^* = \frac{a+b+2c}{a} \tag{5.26}$$

Similar to the inner domain, we also need to test if this finite difference scheme is convergent. By use of Taylor expansion, Eqn.(5.19) becomes

$$\bar{R}^2\frac{\partial\bar{C}}{\partial\tau} - \epsilon(\zeta-1)\left.\frac{\partial\bar{C}}{\partial\zeta}\right|_{\zeta=0}\frac{\partial\bar{C}}{\partial\zeta} = \frac{\partial^2\bar{C}}{\partial\zeta^2} + \frac{1}{\zeta+R_c}\frac{\partial\bar{C}}{\partial\zeta} + O(\Delta\tau,\ \Delta\zeta) \tag{5.27}$$

It is shown that as $\Delta\tau$ and $\Delta\zeta$ approach zero, modified equation given in Eqn.(5.27) is reduced to the original partial differential equation. As a result, this method is consistent. Also, according to the unconditional stability of implicit method, we conclude that the implicit finite difference method is convergent for any $\Delta\tau$ and $\Delta\zeta$.

5.3 COMPARING THE NUMERICAL RESULTS WITH PERTURBATION SOLUTIONS

In this section, we compare the results by the numerical methods with the approximate solutions obtained using perturbation theory. Values of the parameters are from the research by Gade *et al.* [34]. The initial radius of the inner domain R_1^0 is 0.8 mm; the initial radius of the outer domain R_2^0 is 1.58 mm; the radius of the outer insulated boundary R_3 is 10 mm; the saturation solubility C_s is 0.25 g·ml^{-1}, the density of the solid $\rho^s = 285.06$ g·ml^{-1}, and the ratio $\epsilon = C_s/\rho^s = 8.77 \times 10^{-4}$; the diffusion coefficient $D = 2.123 \times 10^{-6}$ mm^{-2}·s^{-1}, and $h = 1.053 \times 10^{-6}$ mm·s^{-1}. Figure 5 and Figure 6 show the first order approximate solutions by perturbation theory and the corresponding numerical results for the inner and outer radiuses, respectively.

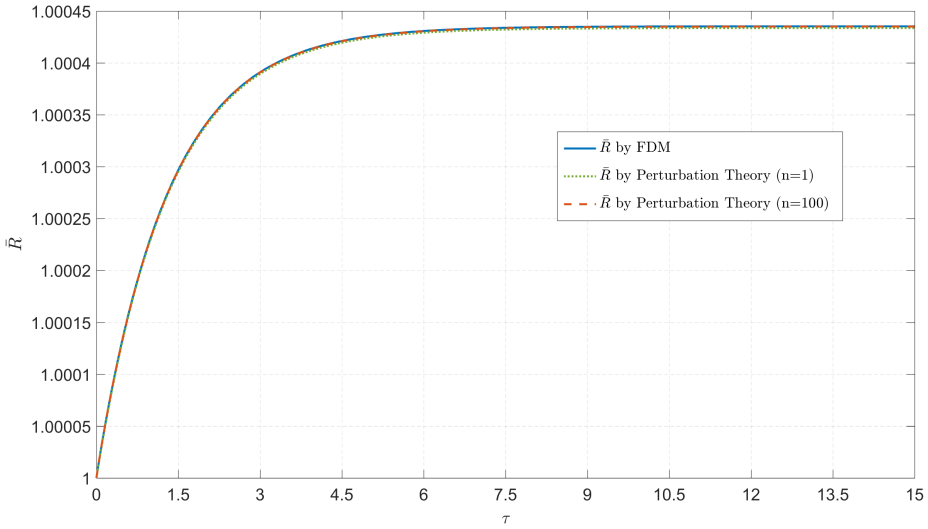


Figure 5: Comparison of the first order perturbation solution with the numerical solution of the non-dimensional inner radius. n is the numbers of terms of the perturbation solution; eigenvalues are computed to four decimal places; $\epsilon = 8.77 \times 10^{-4}$; $\beta = 0.4216$; $\Delta\zeta = 0.0078$; $\Delta\tau$=0.0005; total non-dimensional time=15.

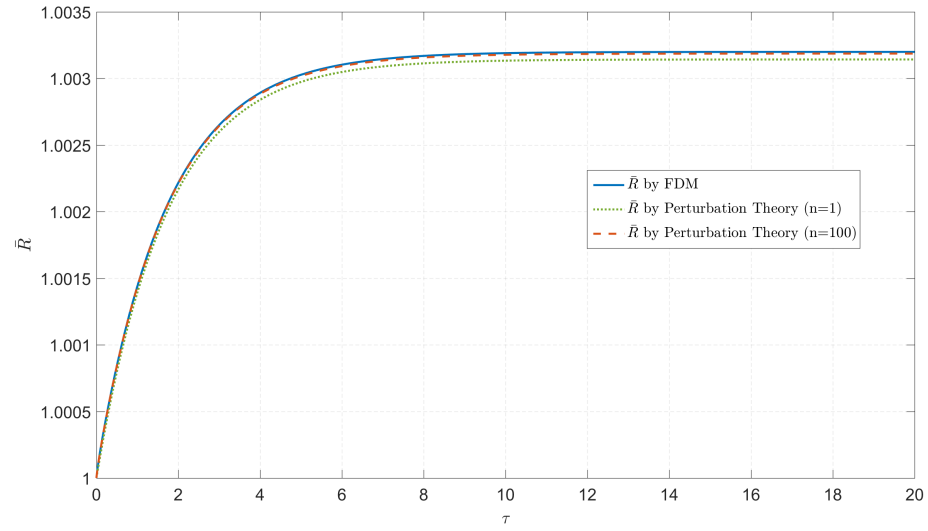


Figure 6: Comparison of the first order perturbation solution with the numerical solution of the non-dimensional outer radius. n is the numbers of terms of the perturbation solution; eigenvalues are computed to four decimal places; $\epsilon = 8.77 \times 10^{-4}$; $\beta = 4.1763$; $\Delta\zeta = 0.0156$; $\Delta\tau$=0.0005; total non-dimensional time=20.

As seen in these figures, the approximate solutions of the radiuses for both the inner and outer domains are dominated by their first term of the solution. Moreover, for the small values of ϵ in the

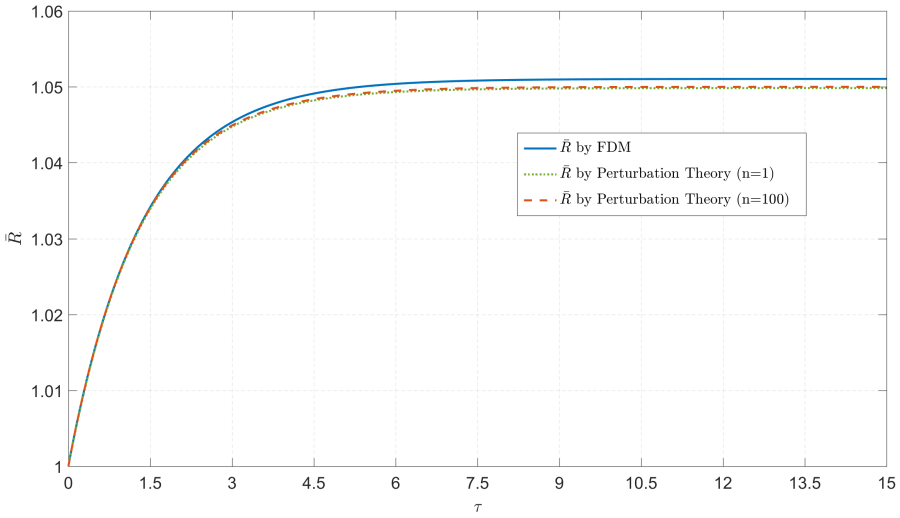
actual experiments, the difference between the first order approximate solutions and the numerical solutions is negligible. This can be explained by the nature of the PDE. As ϵ approaches zero, the second convection term in Eqn.(4.17) and that in Eqn.(4.45) vanish so that the moving boundary problems are reduced to unperturbed problems. However, as ϵ becomes bigger, the difference between approximate solution and numerical solution becomes noticeable. Figure 7 and Figure 8 compare the solutions by the two approaches with larger values of ϵ for the inner domain and the outer domain, respectively. For the inner domain, it is shown that the first order approximate solutions are close to the numerical solutions even for large ϵ. However, for the outer domain, the difference between the approximate solutions and the numerical solutions becomes noticeable for large ϵ. Physically, due to the larger space between R_2 and R_3, shown in Figure 4, the time for the solution to reach its saturation concentration is longer than that for the inner domain. Therefore the change of the outer radius is greater than the inner radius. Since the first order solution of $\bar{R}$ is obtained using the zero$^{\text{th}}$ order solution of $\bar{C}$, which is obtained by making ϵ to be zero and the $\bar{R}$ to be immobile, the accuracy of lower order approximations may not be satisfactory for $\bar{R}$ that changes significantly over time.

In order to better show the accuracy of the approximate solutions, we use

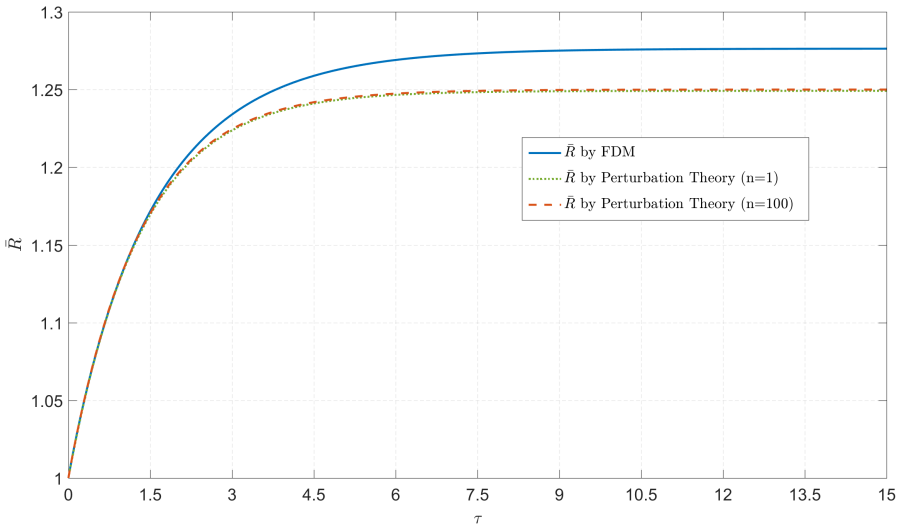
$$P = \max \left| \frac{\bar{R}_{\text{FDM}} - \bar{R}_{\text{Perturbation}}}{\bar{R}(0)} \right| \times 100\% \tag{5.28}$$

to represent the difference between the non-dimensional radius by perturbation theory and that by finite different method for both the inner and the outer domain. Figure 9 and Figure 10 show the relationship between P and ϵ for the inner and outer domains, respectively. Also, the effect of values of β is also investigated.

As indicated in Figure 9 and Figure 10, P is shown to have an approximately positive correlation with ϵ. Surprisingly, P goes down after it reaching a maximum value when $\beta = 10$ for the inner domain. Moreover, it is suggested that there is no obvious relationship between P and β. The error of the solutions by perturbation theory is shown to be small, and the maximum difference by our calculations is 6%, which is acceptable for practical purposes.

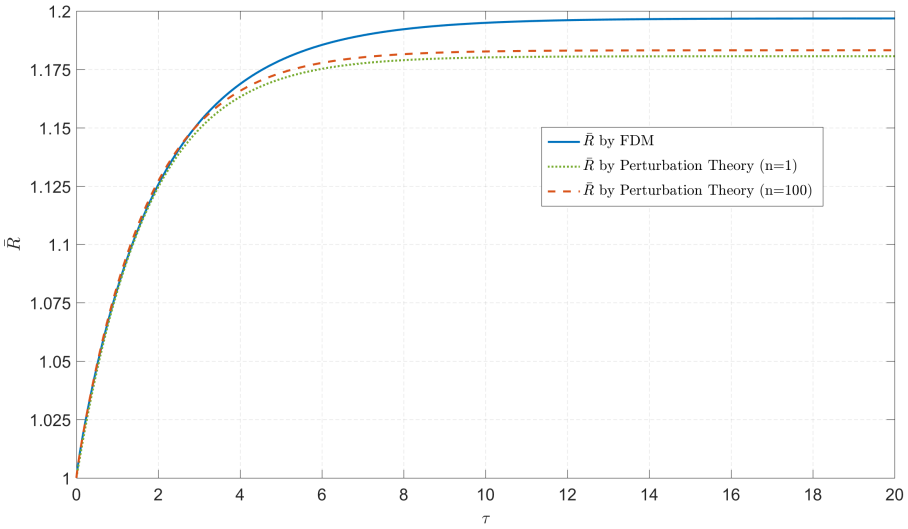


(a) ϵ=0.1

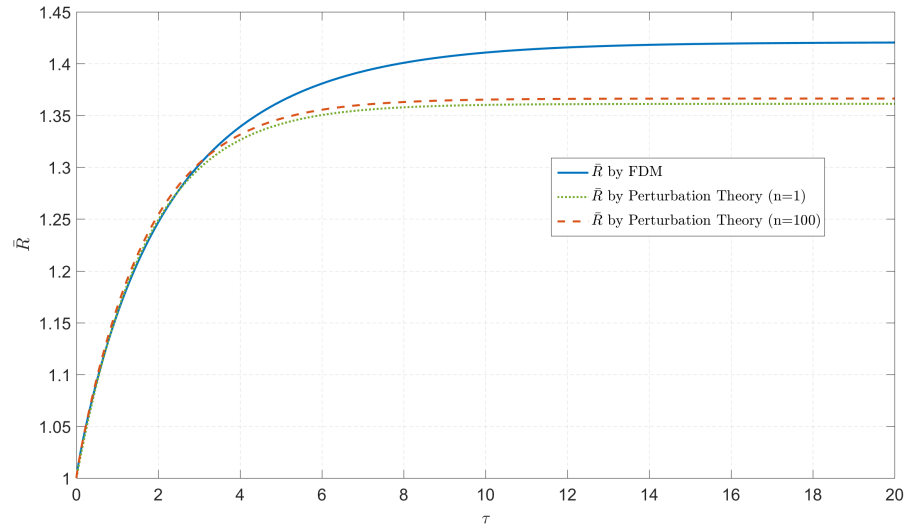


(b) ϵ=0.5

Figure 7: Comparison of the first order perturbation solution with the numerical solution of the non-dimensional inner radius for larger ϵ. n is the numbers of terms of the perturbation solution; eigenvalues are computed to four decimal places; $\beta = 0.4216$; $\Delta\zeta = 0.0078$; $\Delta\tau$=0.0005; total non-dimensional time=15.



(a) ϵ=0.05



(b) ϵ=0.1

Figure 8: Comparison of the first order perturbation solution with the numerical solution of the non-dimensional outer radius for larger ϵ. n is the numbers of terms of the perturbation solution; eigenvalues are computed to four decimal places; $\beta = 4.1763$; $\Delta\zeta = 0.0156$; $\Delta\tau$=0.0005; total non-dimensional time=20.

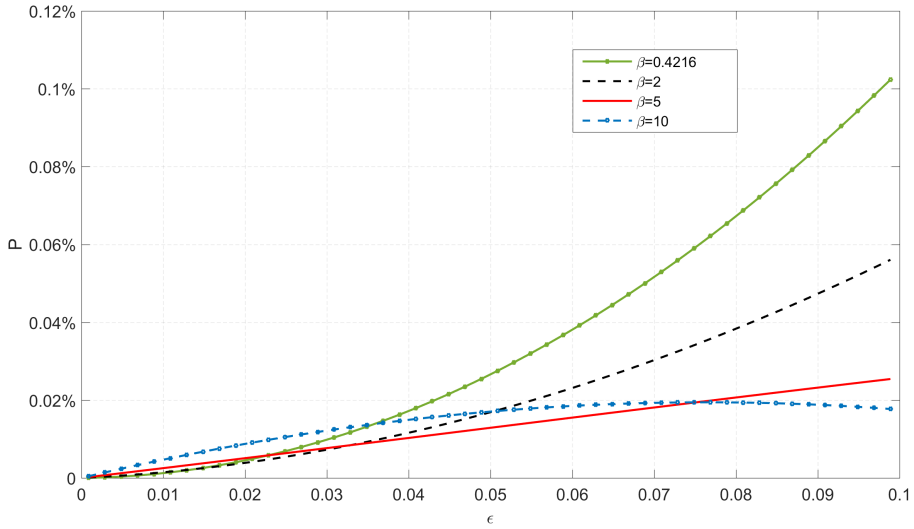


Figure 9: Plot of P of the inner domain against ϵ for different values of β. β is a non-dimensional parameter defined in (4.16); for the summation: number of terms of the perturbation solution $n = 100$; eigenvalues are computed to four decimal places; $\Delta\zeta = 0.0078$; $\Delta\tau$=0.0005; total non-dimensional time=15.

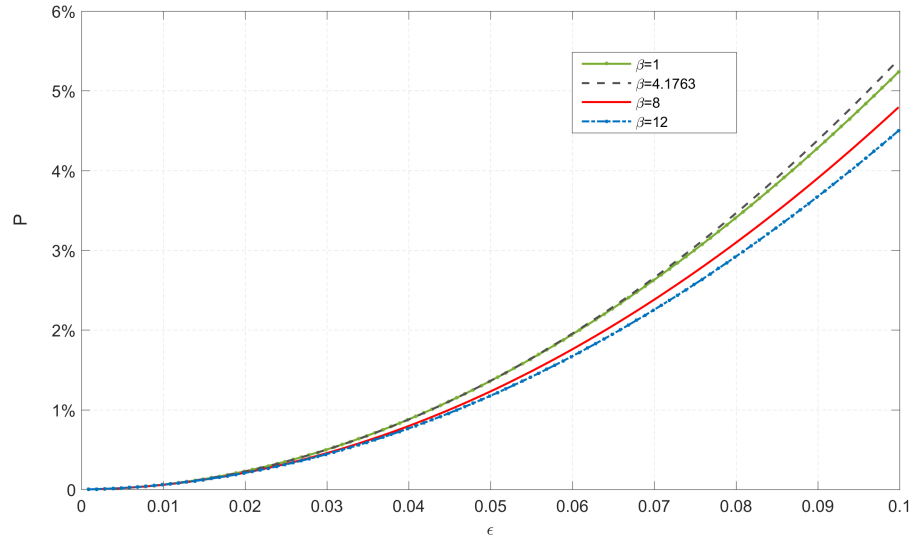


Figure 10: Plot of P of the outer domain against ϵ for different values of β. β is a non-dimensional parameter defined in (4.44); for the summation: number of terms of the perturbation solution $n = 100$; eigenvalues are computed to four decimal places; $\Delta\zeta = 0.0156$; $\Delta\tau$=0.0005; total non-dimensional time=20.

6.0 THE *IN VIVO* PROBLEM

In the above chapters, we deal with the *in vitro* problem that the vascular graft degrades in stationary solvent. However, for the *in vivo* problem, the inner domain experiences blood flow instead of stationary fluid. Moreover, blood vessel reconstitution is involved for the *in vivo* problem. As a result, the problem becomes more complex.

For the outer domain, there is no insulated boundary outside the vascular graft since it is just an analogy to the experimental condition for the *in vitro* problem. We assume that the degradation process is still axisymmetric and governed by simple diffusion without axial effects, and the effect of the cells is negligible for the diffusion process. Therefore the only difference between *in vitro* and *in vivo* degradation for the outer domain is the existence of the outer boundary. Because of the absence of the outer boundary, the problem of the outer domain is now in a semi-infinite region. Although there exist closed form solutions for a few moving boundary problems in semi-infinite regions, the solution to this problem is not found in our study due to the restriction from the Robin boundary condition [24], [25], [38]. As for the *in vitro* problem, we still need to solve this problem in a finite domain since three boundary conditions are required to solve this problem. To this end, one approach is to assume that the gradient of C is zero at positions far from Γ_2, where an imaginary insulated boundary Γ_3 is postulated to serve as a boundary condition.

Unlike the *in vitro* degradation, cellular attachment and growth have to be considered. As the graft degrades, cells replace the position where the graft occupies initially and reconstitute a new blood vessel over time. Figure 11 shows the cross section of a vascular graft containing a cell layer in the inner domain. If we assume that the inner radius of the cell layer R_1 is stationary, the velocity profile inside the graft should remain unchanged. Such that the problem in the inner domain is divided into two sub-problems: pure diffusion problem in the cell layer, and diffusion-convection problem for the inner flow part.

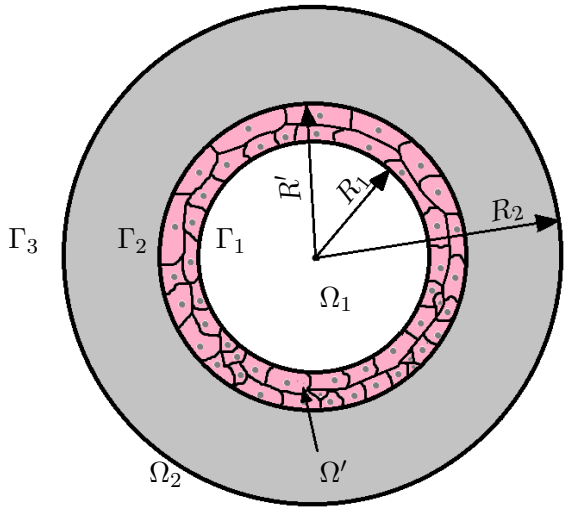


Figure 11: A cross section of a vascular graft containing a cell layer in the inner domain. Γ_1 and Γ_2 represent the inner and the outer surface of the cell layer, respectively; Γ_3 is the outer surface of the graft; Ω_1 represents the flow region; Ω' represents the cell layer; Ω_2 represents the outer domain.

6.1 PROBLEM FOR THE FLOW REGION

For the flow region where Ω_1, the velocity profile is to be determined. Due to the nature of living body, two features need to be concerned: the effect of flow pulsation caused by heart beats; and the fact that blood is non-Newtonian fluid. These two features introduce more complicated mechanism into the problem and we definitely need proper assumptions to simplify them. Caro [39] in his experiment measured the concentration variation of an injected dye in both pulsatile and steady flow. It showed that the effect of pulsation is not notable for bent tubes, and that is small for straight tubes. Therefore in this problem, we neglect the effect of pulsation and assume the flow is steady. Moreover, McDonald [40] showed that for blood with high flow rate (in the arteries, for example), the flow of blood is effectively Newtonian. Therefore for this work, we will assume the flow is axisymmetric and full developed, and the velocity profile follows the form of Poiseuille flow, which is given by

$$u = U_0(1 - \frac{r^2}{{R_1}^2}) \qquad 0 < r < R_1 \tag{6.1}$$

where U_0 is the maximum velocity, which occurs at $r = 0$. By substituting (6.1) into (3.4), we obtain the governing equation for the inner domain as

$$\frac{\partial C}{\partial t} + U_0(1 - \frac{r^2}{{R_1}^2})\frac{\partial C}{\partial x} = D(\frac{1}{r}\frac{\partial C}{\partial r} + \frac{\partial^2 C}{\partial r^2} + \frac{\partial^2 C}{\partial x^2}) \qquad 0 < r < R_1 \tag{6.2}$$

where x is the axial coordinate.

If we use the following non-dimensional parameters and properties to normalize Eqn.(6.2)

$$\bar{C} = \frac{C_s - C}{C_s} \qquad \tau = \frac{U_0 t}{R_1} \qquad \zeta = \frac{r}{R_1} \qquad \eta = \frac{x}{R_1} \qquad \mathrm{Pe} = \frac{U_0 R_1}{D} \tag{6.3}$$

it becomes

$$\frac{\partial \bar{C}}{\partial \tau} + (1 - \zeta^2)\frac{\partial \bar{C}}{\partial \eta} = \frac{1}{\mathrm{Pe}}\left(\frac{1}{\zeta}\frac{\partial \bar{C}}{\partial \zeta} + \frac{\partial^2 \bar{C}}{\partial \zeta^2} + \frac{\partial^2 \bar{C}}{\partial \eta^2}\right) \qquad 0 < r < R_1 \tag{6.4}$$

Since D as found experimentally to be relative small, the Peclet number Pe becomes much greater than one for high-velocity blood flow such as in arteries. Therefore the effect of the diffusion terms in Eqn.(6.4) may be considered as a small perturbation. By letting the right hand side tend to zero, Eqn.(6.4) becomes

$$\frac{\partial \bar{C}}{\partial \tau} + (1 - \zeta^2)\frac{\partial \bar{C}}{\partial \eta} = 0 \qquad 0 < r < R_1 \tag{6.5}$$

and not surprisingly, this is just the pure convection. This conclusion is consistent with the results from the experiment conducted by Bailey and Gogarty [41]. It was shown that for arteries, the dispersion process is dominated by simple convection. Moreover, if the flow rate is high enough, we may consider $C(x, r, t) = 0$ in the flow part for short vascular graft since the concentration profile is close to the inflow in which $C = 0$. With this assumption, the diffusion problem in the cell layer becomes one-dimensional and can be solved by the perturbation theory.

However for low flow rate, Griffiths [42] in his experiment showed that the distribution of concentration over a cross section is almost constant. With this result, Taylor [43] developed a dispersion model base on the mean concentration at every cross section defined by

$$C_m = \frac{2}{{R_1}^2} \int_0^{R_1} Cr \; dr \tag{6.6}$$

which is valid for large values of t. Then Taylor's dispersion model is generalized by Gill and Sankarasubramanian [44] by making a series expansion, making it works for small values of time. Lighthill [45] also made a complement to Taylor's theory by giving a solution valid for small value of t to illustrate the initial action for the diffusion-convection process.

6.2 PROBLEM FOR THE CELL LAYER

In the meantime, the concentration inside the cell layer Ω' is not directly affected by the flow and governed by diffusion only, which is written as

$$\frac{\partial C'}{\partial t} = D'(\frac{1}{r}\frac{\partial C'}{\partial r} + \frac{\partial^2 C'}{\partial r^2} + \frac{\partial^2 C'}{\partial x^2}) \qquad R_1 < r < R' \tag{6.7}$$

where D' denotes the diffusion coefficient inside the cell layer; C' is the concentration inside the cell layer. Similar to the problem in a quiescent fluid studies for the *in vitro* problem, Γ_2 is constrained by two boundary conditions, (3.5) and (3.9). The moving boundary condition at Γ_2 is written as

$$D'\nabla C' \cdot \mathbf{n} = \rho_s \mathbf{v}_{\Gamma_2} \cdot \mathbf{n} \tag{6.8}$$

where $\mathbf{n}$ is the unit normal to Γ_2 that points inward. Fallowing earlier work by Patel [28], we transform (6.8) to simplify the analysis. The radius of Γ_2 is expressed as

$$r = R'(x,t) \tag{6.9}$$

and if we define a new function $\mathcal{F}(x,r,t)$ to describe the position of Γ_2, we may have

$$\mathcal{F} = r - R'(x,t) = 0 \tag{6.10}$$

Moreover, it follows that

$$\mathbf{n} = \frac{\nabla \mathcal{F}}{|\nabla \mathcal{F}|} = \frac{\nabla C'}{|\nabla C'|} \tag{6.11}$$

$$\nabla C' \cdot \mathbf{n} = \frac{\nabla C' \cdot \nabla \mathcal{F}}{|\nabla \mathcal{F}|} = |\nabla C'| \tag{6.12}$$

$$\mathbf{v} \cdot \mathbf{n} = \frac{\mathbf{v} \cdot \nabla \mathcal{F}}{|\nabla \mathcal{F}|} = \frac{\mathbf{v} \cdot \nabla C'}{|\nabla C'|} \tag{6.13}$$

Taking the material derivative of $\mathcal{F}$ and combining (6.13), we have

$$\mathbf{v} \cdot \mathbf{n} = \frac{-\partial \mathcal{F}/\partial t}{\nabla |\mathcal{F}|} = \frac{-\partial C'/\partial t}{|\nabla C'|} \tag{6.14}$$

Next, by use of (6.12) and (6.14), Eqn.(6.8) becomes

$$-D' \nabla C' \cdot \nabla \mathcal{F} = \rho_s \frac{\partial \mathcal{F}}{\partial t} \tag{6.15}$$

By the differentiation of C and $\mathcal{F}$, we may obtain

$$\frac{\partial C'}{\partial x} = \frac{\partial \mathcal{F}/\partial x}{\partial \mathcal{F}/\partial r} \frac{\partial C'}{\partial r} \tag{6.16}$$

With the aid of (6.16), Eqn.(6.15) is expanded to

$$-D' \frac{\partial C'}{\partial r} [1 + (\frac{\partial \mathcal{F}/\partial x}{\partial \mathcal{F}/\partial r})^2] = \rho_s \frac{\partial \mathcal{F}}{\partial t} / \frac{\partial \mathcal{F}}{\partial r} \tag{6.17}$$

Now, since $\mathcal{F}$ is a function defined by (6.10), Eqn.(6.17) is reduced to

$$D' \frac{\partial C'}{\partial r} [1 + (\frac{\partial R'}{\partial x})^2] = \rho_s \frac{\partial R'}{\partial t} \tag{6.18}$$

If the diffusion coefficient of the blood is same as that of the cell layer, both C and $\partial C/\partial r$ are consistent at the interface Γ_1, which serve as implicit boundary conditions. Therefore the equation set for $C(r, x, t)$ for the full problem of the inner domain is

$$\frac{\partial C}{\partial t} + U_0(1 - \frac{r^2}{{R_1}^2})\frac{\partial C}{\partial x} = D(\frac{1}{r}\frac{\partial C}{\partial r} + \frac{\partial^2 C}{\partial r^2} + \frac{\partial^2 C}{\partial x^2}) \qquad 0 < r < R_1,\ t > 0 \tag{6.19}$$

$$\frac{\partial C'}{\partial t} = D'(\frac{1}{r}\frac{\partial C'}{\partial r} + \frac{\partial^2 C'}{\partial r^2} + \frac{\partial^2 C'}{\partial x^2}) \qquad R_1 < r < R'(x,t),\ t > 0 \tag{6.20}$$

$$D'\frac{\partial C'}{\partial r}[1 + (\frac{\partial R'}{\partial x})^2] = \rho_s \frac{\partial R'}{\partial t} \qquad r = R'(x,t),\ t > 0 \tag{6.21}$$

$$-D'\nabla C' \cdot \mathbf{n} = h(C_s - C') \qquad r = R'(x,t),\ t > 0 \tag{6.22}$$

$$C'(R_1, x, t) = C(R_1, x, t) \qquad r = R_1,\ t > 0 \tag{6.23}$$

$$D'\frac{\partial C'}{\partial r} = D\frac{\partial C}{\partial r} \qquad r = R_1,\ t > 0 \tag{6.24}$$

$$C(r, x, 0) = 0 \qquad 0 < r < R_1,\ t = 0 \tag{6.25}$$

$$R'(x, 0) = R_1 \qquad t = 0 \tag{6.26}$$

The solution to this problem is not going to be shown in this thesis since the 2-dimensional moving boundary condition introduces extra difficulty into the problem. Numerical analysis is scheduled to be conducted and the perturbation solution to this problem is also going to be investigated in our future studies.

7.0 DISCUSSION

In this thesis, we solve the *in vitro* problem for erosion of a vascular graft using both the perturbation theory and the numerical methods. It is shown that mixture theory is a powerful tool to simplify problems including biological tissues. In fact, the moving boundary conditions given in (4.6) and (4.11) can also be derived by using the balance of mass without concerning individual constituents. However, for mixtures with more than three constituents or for porous media, the advantage of jump conditions for mixture in deriving moving boundary conditions is irreplaceable.

It is shown that the first order solutions of the radiuses for both the inner and the outer domain are valid and satisfactory. Although we set the values of ϵ to be utmost 0.5, the real value of it is much smaller. For our experiments using PGS as the material for the graft, our group found the order of ϵ is of 10^{-4}, such that the error of first order approximate solution should be less than 1%. One surprising finding is that the errors of the approximate solutions are not shown to have a obvious relationship with β as expected. Especially in the case that $\beta = 10$ for the inner domain shown in Figure 9, the difference between the approximate solutions and the numerical solutions decreases after reaching a peak as ϵ becomes bigger. Although not shown in this thesis, we note that the errors of the approximate solutions for the outer domain increase as the radius of outer boundary R_3 becomes bigger.

At the end of the thesis, the *in vivo* problem with blood flow inside the inner domain is discussed. With several assumptions, the problem for the inner domain is divided into two sub-problems: a simple diffusion process with moving boundary; and a diffusion-convection process in a fixed domain. Prior work suggests that the problem can be reduced to pure convection for high flow rates, while for small flow rates, it may be assumed that the concentration in the fluid part is independent of r. The difficulty of this problem lies in the moving boundary for the cell layer. Since this is an unsteady 2-dimensional problem, the function of the free boundary is now a function of

both x and t. In the future, we will develop an approach for mapping the cell layer domain to a fixed region as was done for the *in vitro* problem. However, if we use $\zeta = r/R'$ to normalize the radius, the axial dependence of R' will make the dimensionless equation extraordinarily complex. In the future, we will continue to explore methods to simplify the formulation. Numerical analysis will be used to test the idealizations.

APPENDIX A

LIST OF SYMBOLS

$\bar{\mathbf{n}}^{\alpha}$	Angular momentum supply rate on singular surface to constituent α	N/m
$\bar{\mathbf{s}}^{\alpha}$	Linear momentum supply rate on singular surface to constituent α	N/m^2
$\bar{\rho}^{\alpha}$	Mass supply rate on singular surface to constituent α	kg/(m^2·s)
$\bar{C}$	Dimensionless concentration	
$\bar{R}$	Dimensionless radius	
$\bar{w}^{\alpha}$	Energy supply rate on singular surface to constituent α	W/m^2
$\boldsymbol{\chi}$	Motion of $\mathbf{X}^{\alpha}$	
Δm	Mass loss per unit length	kg/m
ϵ	Ratio of ρ^s to C_s	
η	Entropy density	J/ (kg·K)
η^{α}	Entropy density of constituent α	J/ (kg·K)
γ	External heat supply	W/ kg
γ^{α}	External heat supply to constituent α	W/ kg
$\hat{\mathbf{m}}^{\alpha}$	Angular momentum supply to constituent α from other constituents	N/ m^2

$\hat{\mathbf{p}}^{\alpha}$	Momentum supply to constituent α from other constituents	N/ m^3
$\hat{\rho}^{\alpha}$	Mass supply rate to constituent α	kg/(m^3·s)
$\hat{\varepsilon}^{\alpha}$	Energy supply to constituent α from other constituents	W/ m^3
$\mathbf{a}$	Acceleration	m/s^2
$\mathbf{a}^{\alpha}$	Acceleration of constituent α	m/s^2
$\mathbf{b}$	Body force density	N/ kg
$\mathbf{b}^{\alpha}$	Body force density of constituent α	N/ kg
$\mathbf{D}$	Matrix of diffusion coefficient	m^2/s
$\mathbf{F}$	Mass flux vector	kg/(m^2· s)
$\mathbf{q}$	Heat flux vector	W/ m^3
$\mathbf{q}^{\alpha}$	Heat flux vector for constituent α	W/ m^3
$\mathbf{q}_{\mathrm{I}}$	Inner part of heat flux vector	W/ m^3
$\mathbf{T}$	Cauchy stress tensor	N/ m^3
$\mathbf{T}^{\alpha}$	Cauchy stress tensor of constituent α	N/ m^3
$\mathbf{T}_{\mathrm{I}}$	Internal part of Cauchy stress tensor	N/ m^3
$\mathbf{u}^{\alpha}$	Diffusion velocity of constituent α	m/s
$\mathbf{v}$	Velocity	m/s
$\mathbf{v}^{\alpha}$	Velocity of constituent α	m/s
$\mathbf{v}^{\Gamma}$	Velocity of surface γ	m/s
$\mathbf{x}$	The position vector of $\mathbf{X}^{\alpha}$	
$\mathbf{X}^{\alpha}$	A material point of constituent α	
$\mathcal{B}$	A deformable continuous body	
$\mathcal{R}$	A Euclidean space	

$\mathcal{V}$	An arbitrary material region	
$\mathcal{V}^\alpha$	The material region of constituent α coincident with $\mathcal{V}$	
ψ	Helmholtz free energy of constituent α	W/ m^3
ρ	Density	kg/m^3
ρ^α	Apparent density of constituent α	kg/m^3
τ	Dimensionless time	
ε	Internal energy density	J/ kg
ε^α	Internal energy density of constituent α	J/ kg
ζ	Dimensionless radical axis of cylinder coordinate	
C	Concentration	kg/m^3
C_s	Saturation solubility	kg/m^3
D	Diffusion coefficient	m^2/s
h	Material coefficient used in boundary condition	m/s
R	Radius	m
r, x	Radical and axial axis of cylinder coordinate	m
s	Solid	
t	Time	s
u	Solute	
V	Current configuration of $\mathcal{B}$	
V_0	Initial configuration of $\mathcal{B}$	
w	Solvent	

APPENDIX B

GRID SENSITIVITY TEST FOR NUMERICAL METHODS

To ensure the mesh quality, grid sensitivity is analyzed for the numerical methods. Once a difference method is proved to be convergent, the accuracy of the method is mainly determined by grids. Generally, a finer grid gives more details than the coarser ones. However, formulations with higher density mesh require more time to solve. Therefore we consider the mesh to be satisfactory when the results in the same position at fixed time do not significantly change. In this one-dimensional problem, the radius is divided into 2^I grids evenly, where $I = 1, 2, 3, ...$ The residual for the numerical results is described by the second norm which is defined by

$$Re_I = ||C_I - C_{I+1}|| = \left[\sum_i^N (C_i^I - C_{i'}^{I+1})^2\right]^{1/2} \tag{B.1}$$

where i' represents the same position that i occupies. The grid size and the time step are determined in this way: first we choose an arbitrary time step $\Delta\tau$, and we find the optimized ζ by the residuals between two discretization levels; then the grid size is fixed to $\Delta\zeta$ that we find in the previous step, and we determine the optimized time step. As shown in Figure 12 and Figure 13, the optimized time step and the optimized grid size are 0.0005 and $1/2^7$, respectively. Likewise, for the outer domain, we determine the optimized time step and grid size to be 0.0005 and $1/2^6$ according to Figure 14 and 15.

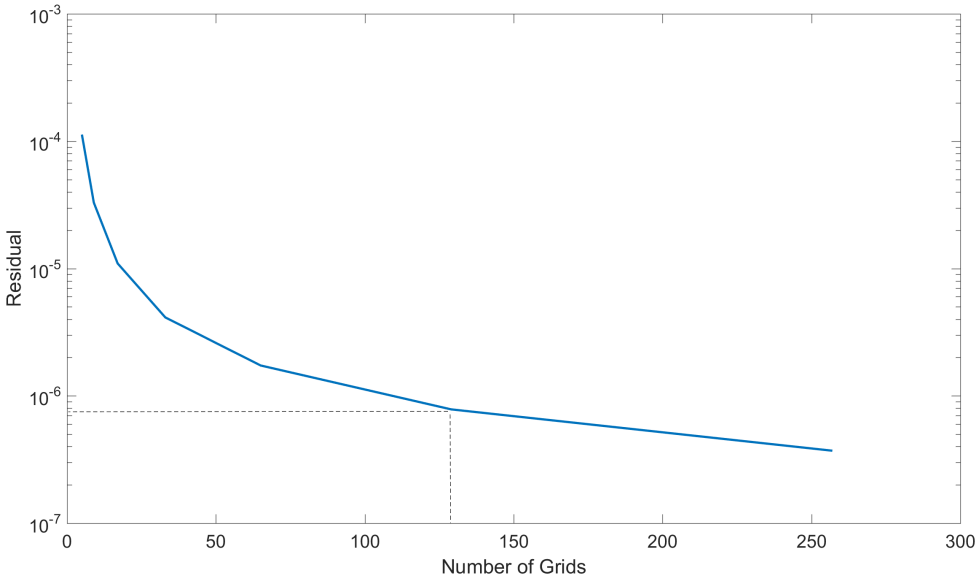


Figure 12: Relationship between the residual and $\Delta\zeta$ for the inner domain. ϵ=0.05, $\Delta\tau$=0.01, total non-dimensional time=5.

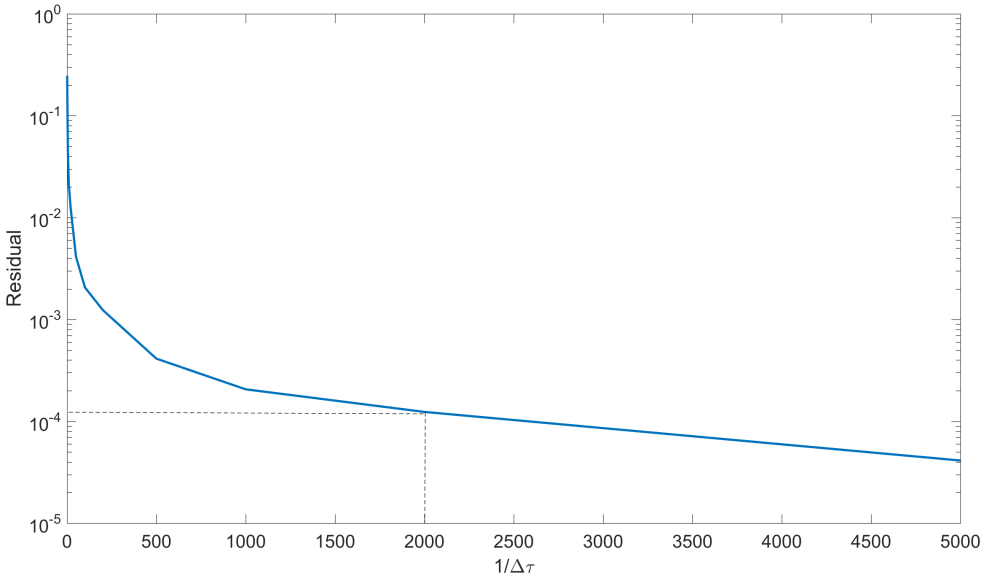


Figure 13: Relationship between the residual and $\Delta\tau$ for the inner domain. ϵ=0.05, $\Delta\zeta = 1/2^7$, total non-dimensional time=5.

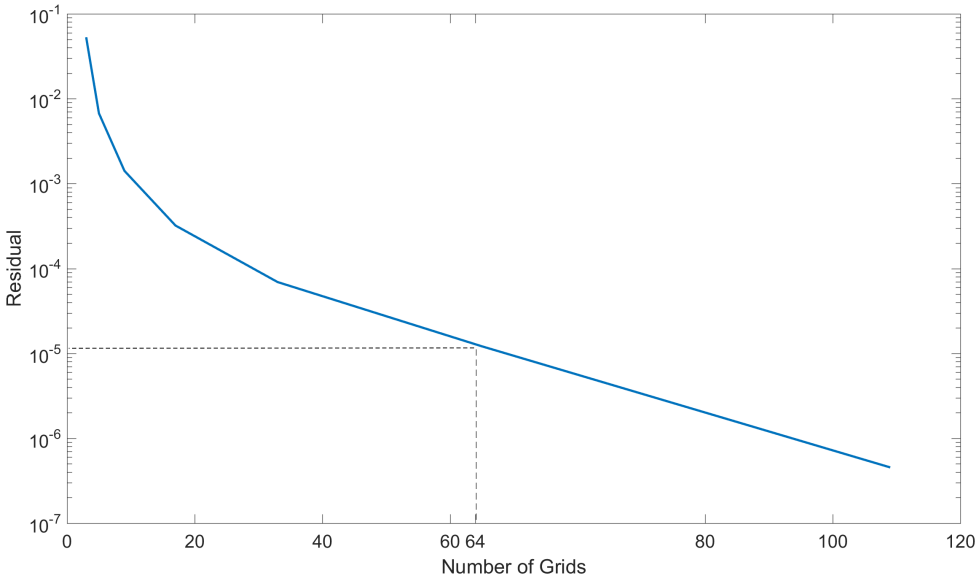


Figure 14: Relationship between the residual and $\Delta\zeta$ for the outer domain. ϵ=0.05, $\Delta\tau$=0.01, total non-dimensional time=5.

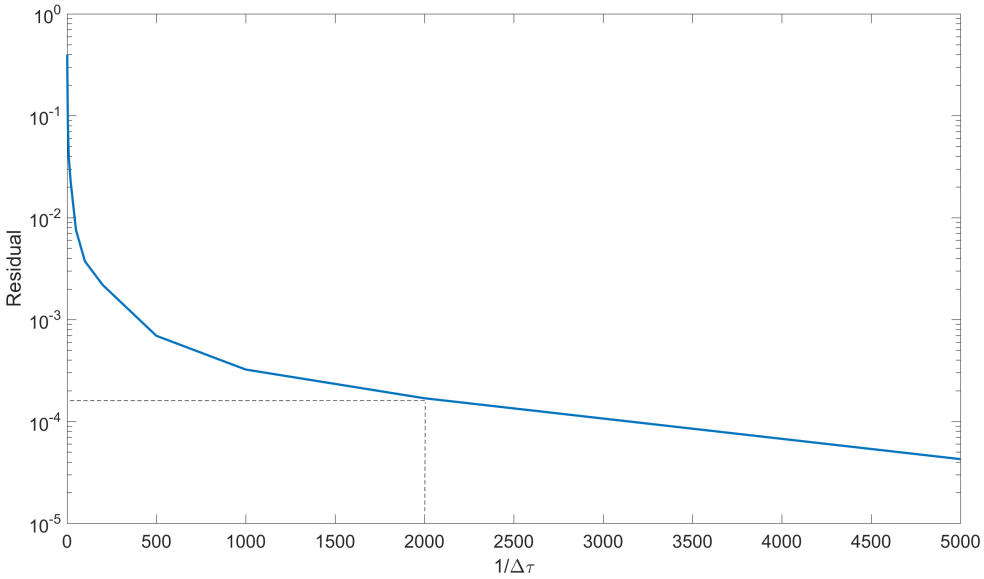


Figure 15: Relationship between the residual and $\Delta\tau$ for the outer domain. ϵ=0.05, $\Delta\zeta = 1/2^6$, total non-dimensional time=5.

APPENDIX C

DERIVATION FOR (2.15)

According to (C.6), we have

$$\rho\frac{Df}{Dt}=\sum_{\alpha}\frac{D(\rho^{\alpha}f^{\alpha})}{Dt} \tag{C.1}$$

By use of the identities in (2.5) and (2.6), we obtain

$$\frac{D(\rho^{\alpha}f^{\alpha})}{Dt}=\frac{D^{\alpha}(\rho^{\alpha}f^{\alpha})}{Dt}-\nabla(\rho^{\alpha}f^{\alpha})\cdot\mathbf{v}^{\alpha}+\nabla(\rho^{\alpha}f^{\alpha})\cdot\mathbf{v} \tag{C.2}$$

Therefore

$$\rho\frac{Df}{Dt}=\sum_{\alpha}\left[\frac{D^{\alpha}(\rho^{\alpha}f^{\alpha})}{Dt}-\nabla(\rho^{\alpha}f^{\alpha})\cdot\mathbf{v}^{\alpha}+\nabla(\rho^{\alpha}f^{\alpha})\cdot\mathbf{v}\right] \tag{C.3}$$

With the aid of (2.13) and (2.16), by expanding the first term in the right of (C.3), we have

$$\rho\frac{Df}{Dt}=\sum_{\alpha}\left[\rho^{\alpha}\frac{D^{\alpha}f^{\alpha}}{Dt}+f^{\alpha}(\hat{\rho}^{\alpha}-\rho^{\alpha}\nabla\cdot\mathbf{v}^{\alpha})-\nabla(\rho^{\alpha}f^{\alpha})\cdot\mathbf{v}^{\alpha}+\nabla(\rho^{\alpha}f^{\alpha})\cdot(\mathbf{v}^{\alpha}-\mathbf{u}^{\alpha})\right] \tag{C.4}$$

Since $\nabla\cdot\mathbf{v}=0$ for incompressible fluid, we get

$$\nabla\cdot\mathbf{v}^{\alpha}=\nabla\cdot\mathbf{u}^{\alpha} \tag{C.5}$$

Thus (C.4) is reduced to

$$\rho \frac{Df}{Dt} = \sum_{\alpha} \rho^{\alpha} \frac{D^{\alpha} f^{\alpha}}{Dt} - \nabla \cdot (\rho^{\alpha} f^{\alpha} \mathbf{u}^{\alpha}) + \hat{\rho}^{\alpha} f^{\alpha} \tag{C.6}$$

APPENDIX D

DERIVATION FOR (2.17)

By taking the summation of Eqn.(2.13) over all constituents, with the identity given in (2.11), we obtain

$$\sum_{\alpha} \frac{D^{\alpha}\rho^{\alpha}}{Dt} + \sum_{\alpha} \rho^{\alpha} \nabla \cdot \mathbf{v}^{\alpha} = 0 \tag{D.1}$$

By use of (2.5) and (2.6), we have

$$\frac{D^{\alpha}\rho^{\alpha}}{Dt} = \frac{D\rho^{\alpha}}{Dt} - \nabla\rho^{\alpha} \cdot \mathbf{v} + \nabla\rho^{\alpha} \cdot \mathbf{v}^{\alpha} \tag{D.2}$$

With (D.2) and (2.8), (D.1) can be written as

$$\frac{D\rho}{Dt} - \nabla\rho \cdot \mathbf{v} + \sum_{\alpha} \nabla \cdot (\rho^{\alpha}\mathbf{v}^{\alpha}) \tag{D.3}$$

By use of the identity given in (2.18), (D.3) becomes

$$\frac{D\rho}{Dt} + \rho \nabla \cdot \mathbf{v} = 0 \tag{D.4}$$

APPENDIX E

DERIVATION FOR (2.22)

With (2.5), (2.6) and (2.16), we shall have

$$\frac{D\mathbf{v}^\alpha}{Dt} = \frac{D^\alpha \mathbf{v}^\alpha}{Dt} - (\nabla \mathbf{v}^\alpha) \cdot \mathbf{u}^\alpha \tag{E.1}$$

By use of (2.18), $\rho\mathbf{a}$ can be expanded to

$$\begin{aligned}
\rho\mathbf{a} &= \rho \frac{D\mathbf{v}}{Dt} \\
&= \rho \frac{D\frac{1}{\rho}\sum_\alpha \rho^\alpha \mathbf{v}^\alpha}{Dt} \\
&= \sum_\alpha [\rho^\alpha \mathbf{a}^\alpha - \rho^\alpha \nabla \mathbf{v}^\alpha \cdot \mathbf{u}^\alpha + \mathbf{v}^\alpha (\hat{\rho}^\alpha - \rho^\alpha \nabla \cdot \mathbf{v}^\alpha - \mathbf{u}^\alpha \cdot \nabla \rho^\alpha)]
\end{aligned} \tag{E.2}$$

Since

$$\sum_\alpha \mathbf{v}\hat{\rho}^\alpha = \mathbf{v} \sum_\alpha \hat{\rho}^\alpha = 0 \tag{E.3}$$

(E.2) can be reduced to

$$\rho\mathbf{a} = \sum_\alpha [\rho^\alpha \mathbf{a}^\alpha + \hat{\rho}^\alpha \mathbf{u}^\alpha - \nabla \cdot (\rho^\alpha \mathbf{v}^\alpha \otimes \mathbf{u}^\alpha)] \tag{E.4}$$

The second term inside parenthesis in the right hand side of (E.4) can be expanded to

$$\nabla \cdot (\rho^\alpha \mathbf{v}^\alpha \otimes \mathbf{u}^\alpha) = \nabla \cdot (\rho^\alpha \mathbf{u}^\alpha \otimes \mathbf{u}^\alpha) + \nabla \cdot (\rho^\alpha \mathbf{v} \otimes \mathbf{u}^\alpha) \tag{E.5}$$

where according to the identity of incompressible fluid, it can be shown that

$$\sum_\alpha \nabla \cdot (\rho^\alpha \mathbf{v} \otimes \mathbf{u}^\alpha) = \mathbf{0}$$

Thus we have

$$\rho \mathbf{a} = \sum_\alpha [\rho^\alpha \mathbf{a}^\alpha + \hat{\rho}^\alpha \mathbf{u}^\alpha - \nabla \cdot (\rho^\alpha \mathbf{u}^\alpha \otimes \mathbf{u}^\alpha)] \tag{E.6}$$

By taking the summation of Eqn.(2.21) over all constituents, with (2.24)-(2.27), and (E.6), we get

$$\rho \mathbf{a} = \nabla \cdot \mathbf{T} + \rho \mathbf{b} \tag{E.7}$$

APPENDIX F

DERIVATION FOR (2.67)

According to the definition given in (2.51), by use of identity (2.5), we have

$$\rho\frac{D\varepsilon_{\mathrm{I}}}{Dt}=\sum_{\alpha}[\rho^{\alpha}\frac{D^{\alpha}\varepsilon^{\alpha}}{Dt}-\nabla\cdot(\rho^{\alpha}\varepsilon^{\alpha}\mathbf{u}^{\alpha})+\hat{\rho}^{\alpha}\varepsilon^{\alpha}] \tag{F.1}$$

and therefore

$$\sum_{\alpha}\rho^{\alpha}\frac{D^{\alpha}\varepsilon^{\alpha}}{Dt}=\rho\frac{D\varepsilon_{\mathrm{I}}}{Dt}+\sum_{\alpha}[\nabla\cdot(\rho^{\alpha}\varepsilon^{\alpha}\mathbf{u}^{\alpha})-\hat{\rho}^{\alpha}\varepsilon^{\alpha}] \tag{F.2}$$

Substituting (F.2) into (2.46) and taking the summation for both sides, we get

$$\rho\frac{D\varepsilon_{\mathrm{I}}}{Dt}+\sum_{\alpha}[\nabla\cdot(\rho^{\alpha}\varepsilon^{\alpha}\mathbf{u}^{\alpha}+\mathbf{q}^{\alpha})]-\sum_{\alpha}\hat{\rho}^{\alpha}\varepsilon^{\alpha}=\sum_{\alpha}\mathbf{T}^{\alpha}:\nabla\mathbf{v}^{\alpha}+\rho r+\sum_{\alpha}\hat{\varepsilon}^{\alpha} \tag{F.3}$$

and this can be written as

$$\rho\frac{D\varepsilon_{\mathrm{I}}}{Dt}-\sum_{\alpha}\hat{\rho}^{\alpha}\varepsilon^{\alpha}-\sum_{\alpha}\hat{\varepsilon}^{\alpha}=\sum_{\alpha}\mathbf{T}^{\alpha}:\nabla\mathbf{v}^{\alpha}-\nabla\cdot\mathbf{k}+\rho r \tag{F.4}$$

If the body force is uniform, according to Eqn.(2.62), (F.4) becomes

$$\sum_{\alpha}\mathbf{T}^{\alpha}:\nabla\mathbf{v}^{\alpha}-\nabla\cdot\mathbf{k}+\rho r=\rho\frac{D\varepsilon_{\mathrm{I}}}{Dt}+\sum_{\alpha}\mathbf{u}^{\alpha}\cdot\hat{\mathbf{p}}^{\alpha}+\frac{1}{2}\sum_{\alpha}\hat{\rho}^{\alpha}\mathbf{u}^{\alpha}\cdot\mathbf{u}^{\alpha} \tag{F.5}$$

By combining (F.4) and (F.5), we obtain

$$\sum_{\alpha}[\hat{\varepsilon}^{\alpha} + \mathbf{u}^{\alpha} \cdot \hat{\mathbf{p}}^{\alpha} + \hat{\rho}^{\alpha}(\hat{\varepsilon}^{\alpha} + \frac{1}{2}\mathbf{u}^{\alpha} \cdot \mathbf{u}^{\alpha})] = 0 \tag{F.6}$$

Namely,

$$\sum_{\alpha} \hat{e}^{\alpha} = 0 \tag{F.7}$$

APPENDIX G

DERIVATION FOR (4.39)

For the 0^{th} order problem of the inner domain given in (4.35)-(4.38), by separation of variables, we propose that

$$\bar{C_0} = X(\zeta)T(\tau) \tag{G.1}$$

By substituting this expression into (4.35), we have

$$\frac{T'}{T} = \frac{X'' + X'/(\zeta)}{X} = -\alpha^2 \tag{G.2}$$

Therefore

$$T(\tau) = Ae^{-\alpha^2\tau} \tag{G.3}$$

$$X(\zeta) = BJ_0(\alpha\zeta) + CY_0(\alpha\zeta) \tag{G.4}$$

Because $X(\zeta)$ is bounded at $\zeta = 0$,

$$C = 0 \tag{G.5}$$

By applying the convective boundary condition, we get

$$\alpha_n J_1(\alpha_n) = \beta J_0(\alpha_n) \tag{G.6}$$

and this is th eigrnfunvtion for α_ns.

Therefore

$$\bar{C_0} = T(\tau)X(\zeta) = \sum_{n=1}^{\infty} D_n J_0(\alpha_n \zeta) e^{-{\alpha_n}^2 \tau} \tag{G.7}$$

By applying the initial condition into (G.7), we have

$$\bar{C_0} = \sum_{n=1}^{\infty} D_n J_0(\alpha \zeta) = 1 \tag{G.8}$$

Next, by multiplying both sides of (G.8) by $\zeta J_0(\alpha_m \zeta)$ and integrating the equation from 0 to 1, we have

$$\int_0^1 \sum_{n=1}^{\infty} \zeta D_n J_0(\alpha_n \zeta) J_0(\alpha_m \zeta) d\zeta = \int_0^1 \zeta J_0(\alpha_m \zeta) d\zeta \tag{G.9}$$

According to the orthogonal property of Bessel functions and the eigenfunction, we have

$$D_n = \frac{2\beta}{({\alpha_n}^2 + \beta^2) J_0(\alpha_n)} \tag{G.10}$$

Thus

$$\bar{C_0} = \sum_{n=1}^{\infty} \frac{2\beta J_0(\alpha_n \zeta)}{(\alpha_n^2 + \beta^2) J_0(\alpha_n)} e^{-{\alpha_n}^2 \tau} \tag{G.11}$$

APPENDIX H

DERIVATION FOR (4.55)

Following the same procedure in Appendix G, by separation of variables, assume that

$$\bar{C}_0 = X(\zeta)T(\tau) \tag{H.1}$$

By substituting (H.1) into (4.51), we have

$$\frac{T'}{T} = \frac{X'' + X'/(\zeta + \bar{a})}{X} = -\alpha^2 \tag{H.2}$$

Thus

$$T = Ee^{-\alpha^2 \tau} \tag{H.3}$$

$$X = AJ_0[\alpha(\zeta + \bar{a})] + BY_0[\alpha(\zeta + \bar{a})] \tag{H.4}$$

By using boundary condition (4.53), the relationship between the two coefficients A and B is obtained as

$$B = -\frac{AJ_1(\alpha\bar{a} + \alpha)}{Y_1(\alpha\bar{a} + \alpha)} \tag{H.5}$$

Therefore the expression of X can be rewritten as

$$X = AJ_0[\alpha(\zeta+\bar{a})] - \frac{AJ_1(\alpha\bar{a}+\alpha)}{Y_1(\alpha\bar{a}+\alpha)}Y_0[\alpha(\zeta+\bar{a})]$$
$$= E\{Y_1(\alpha\bar{a}+\alpha)J_0[\alpha(\zeta+\bar{a})] - J_1(\alpha\bar{a}+\alpha)Y_0[\alpha(\zeta+\bar{a})]\} \tag{H.6}$$

By substituting (H.6) into the boundary condition in (4.52), we obtain the eigenfunction as

$$-\alpha_n[J_1(\alpha\alpha_n)Y_1(\alpha_n\bar{a}+\alpha) - Y_1(\alpha\alpha_n)J_1(\alpha_n\bar{a}+\alpha)] =$$
$$\beta[Y_1(\alpha_n\bar{a}+\alpha)J_0(\alpha\alpha_n) - J_1(\alpha+\alpha_n\bar{a})Y_0(\alpha\alpha_n)] \tag{H.7}$$

For convenience, let

$$\phi[\alpha(\zeta+\bar{a})] = Y_1(\alpha\bar{a}+\alpha)J_0[\alpha(\zeta+\bar{a})] - J_1(\alpha\bar{a}+\alpha)Y_0[\alpha(\zeta+\bar{a})] \tag{H.8}$$

Therefore

$$\bar{C}_0 = \sum_{n=1}^{\infty} X_n T_n = \sum_{n=1}^{\infty} D_n\phi[\alpha_n(\zeta+\bar{a})]e^{-\alpha_n^2\tau} \tag{H.9}$$

Substituting the initial condition into (H.9), we get

$$\sum_{n=1}^{\infty} D_n\phi[\alpha_n(\zeta+\bar{a})] = 1 \tag{H.10}$$

Multiplying the equation by $(\zeta+\bar{a})\phi[\alpha_m(\zeta+\bar{a})]$ and integrating from 0 to 1, (H.10) becomes

$$\int_0^1 \sum_{n=1}^{\infty} D_n(\zeta+\bar{a})\phi[\alpha_n(\zeta+\bar{a})]\phi[\alpha_m(\zeta+\bar{a})]\, d\zeta = \int_0^1 (\zeta+\bar{a})\phi[\alpha_m(\zeta+\bar{a})]\, d\zeta \tag{H.11}$$

and this equation can be simplified by the orthogonal properties of Bessel functions. To this end, we define

$$u = \phi[\alpha_n(\zeta+\bar{a})] \tag{H.12}$$
$$v = \phi[\alpha_m(\zeta+\bar{a})] \tag{H.13}$$

where α_n and α_m are two of the roots of Eqn.(H.7). Moreover, according (H.2), u and v are

subjected to

$$(\zeta + \bar{a})u'' + u' + {\alpha_n}^2 \zeta u = 0 \tag{H.14}$$

$$(\zeta + \bar{a})v'' + v' + {\alpha_m}^2 \zeta v = 0 \tag{H.15}$$

which is equivalent to

$$[(\zeta + \bar{a})u']' + {\alpha_n}^2 (\zeta + \bar{a})u = 0 \tag{H.16}$$

$$[(\zeta + \bar{a})v']' + {\alpha_m}^2 (\zeta + \bar{a})v = 0 \tag{H.17}$$

Multiplying (H.16) and (H.17) by v and u respectively, by subtracting the two equations and rearranging terms, we have

$$({\alpha_n}^2 - {\alpha_m}^2)(\zeta + \bar{a})uv = [u(\zeta + \bar{a})v' - v(\zeta + \bar{a})u']' \tag{H.18}$$

Next, by integrating (H.18) from 0 to 1, it becomes

$$({\alpha_n}^2 - {\alpha_m}^2) \int_0^1 (\zeta + \bar{a})uv \, d\zeta = [u(\zeta + \bar{a})v' - v(\zeta + \bar{a})u' \,]|_0^1 \tag{H.19}$$

The right hand side of (H.19) is

$$\begin{aligned} &[u(\zeta + \bar{a})v' - v(\zeta + \bar{a})u' \,]|_0^1 \\ &= (1 + \bar{a})u(1)v'(1) - (1 + \bar{a})v(1)u'(1) - \bar{a}u(0)v'(0) + \bar{a}v(0)u'(0) \\ &= 0 \end{aligned} \tag{H.20}$$

Thus for any $\alpha_n \neq \alpha_m$, $\int_0^1 (\zeta + \bar{a})uv \, d\zeta$ is equal to 0. Namely,

$$\int_0^1 (\zeta + \bar{a})\phi[\alpha_n(\zeta + \bar{a})]\phi[\alpha_m(\zeta + \bar{a})] \, d\zeta = 0 \qquad \alpha_n \neq \alpha_m \tag{H.21}$$

Next, by multiplying (H.14) by $2u'(\zeta + \bar{a})$, we get

$$2(\zeta + \bar{a})^2 u''u' + 2(\zeta + \bar{a}){u'}^2 + 2\alpha_n^2(\zeta + \bar{a})^2 uu' = 0 \tag{H.22}$$

which can be rewritten as

$$[(\zeta+\bar{a})^2 u'^2 + (\zeta+\bar{a})^2 \alpha_n^2 u^2]' - 2(\zeta+\bar{a})\alpha_n^2 u^2 = 0 \tag{H.23}$$

By integrating (H.23) from 0 to 1, we obtain

$$[(\zeta+\bar{a})^2 u'^2 + (\zeta+\bar{a})^2 \alpha_n^2 u^2]|_0^1 = 2\alpha_n^2 \int_0^1 (\zeta+\bar{a})u^2 \, d\zeta \tag{H.24}$$

Therefore we have

$$\int_0^1 (\zeta+\bar{a})u^2 \, d\zeta = \frac{(1+\bar{a})^2 {\alpha_n}^2 u^2[\alpha_n(1+\bar{a})] - \bar{a}^2(\beta^2+{\alpha_n}^2)u^2(\alpha_n\bar{a})}{2\alpha_n^2} \tag{H.25}$$

Namely,

$$\int_0^1 (\zeta+\bar{a})\phi^2[\alpha_n(\zeta+\bar{a})] \, d\zeta = \frac{(1+\bar{a})^2 {\alpha_n}^2 \phi^2[\alpha_n(1+\bar{a})] - \bar{a}^2(\beta^2+{\alpha_n}^2)\phi^2(\alpha_n\bar{a})}{2\alpha_n^2} \tag{H.26}$$

Combining Eqn.(H.11), we have

$$D_n = \frac{2\bar{a}\beta\phi(\bar{a}\alpha_n)}{(1+\bar{a})^2 {\alpha_n}^2 \phi^2[\alpha_n(1+\bar{a})] - \bar{a}^2(\beta^2+{\alpha_n}^2)\phi^2(\alpha_n\bar{a})} \tag{H.27}$$

APPENDIX I

EIGENVALUES FOR THE APPROXIMATE SOLUTIONS

Table 1: First twenty eigenvalues of (4.40) for the *in vitro* approximate solutions of the inner domain ($\beta = 0.4216$).

n	α_n	Value of α_n
1	α_1	0.8720
2	α_2	3.9398
3	α_3	7.07540
4	α_4	10.2148
5	α_5	13.3553
6	α_6	16.4962
7	α_7	19.6373
8	α_8	22.7786
9	α_9	25.9199
10	α_{10}	29.0613
11	α_{11}	32.2028
12	α_{12}	35.3442
13	α_{13}	38.4857
14	α_{14}	41.6272
15	α_{15}	44.7687
16	α_{16}	47.9103
17	α_{17}	51.0518
18	α_{18}	54.1933
19	α_{19}	57.3349
20	α_{20}	60.4764

Table 2: First twenty eigenvalues of (4.57) for the *in vitro* approximate solutions of the outer domain ($\beta = 4.1763$).

n	α_n	Value of α_n
1	α_1	0.7646
2	α_2	3.9185
3	α_3	6.8983
4	α_4	9.9151
5	α_5	12.9673
6	α_6	16.0443
7	α_7	19.1380
8	α_8	22.2429
9	α_9	25.3558
10	α_{10}	28.4744
11	α_{11}	31.5971
12	α_{12}	34.7230
13	α_{13}	37.8514
14	α_{14}	40.9817
15	α_{15}	44.1135
16	α_{16}	47.2466
17	α_{17}	50.3807
18	α_{18}	53.5157
19	α_{19}	56.6513
20	α_{20}	59.7876

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